

A TEXTBOOK OF ORGANIC CHEMISTRY

(Second Edition)

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Preface to the Second Edition

The *first edition* of this book which appeared in 1985 was approved for a subsidy grant by the National Book Trust of India, New Delhi. A reprint was published subsequently in the following year. The wide acceptance of the *first edition* over a period of five years has encouraged me to continue my efforts to improve the effectiveness of this book as a teaching text. Moreover, the need for refinements of certain portions of the book, as pointed out by the readers from time to time, and fascinating important developments have prompted me to undertake a revision of the *Textbook of Organic Chemistry*. The book now hopefully will meet the curriculum requirements adequately for students at the undergraduate level and allied sciences of a large number of Universities. It is designed as a comprehensive textbook and not a reference book.

The overall organization of the book which has been found pedagogically useful, has been retained. For the *second edition*, however, I have worked to improve further the readability of the text. A great deal of material has been added to almost all the chapters. The information on polymers which was interspersed throughout the book in the earlier edition now has been collected into a single chapter. The basic principles are discussed early in the book. A sound foundation of these principles would provide the students with the necessary background for a deeper understanding of the material in the subsequent chapters. The book thus commences with an introductory chapter (*Chapter 1*) on the electronic structure of the atom, nature of chemical bonding and hybridization. The concept of hybridization and the section on H-bonding has been expanded to make them more intelligible. Furthermore, at an early stage a chapter (*Chapters 2 to 5*) each on nomenclature of organic compounds, factors that affect acid-base strength, stereochemistry and reaction mechanisms have been introduced. The IUPAC nomenclature has been further developed in an attempt to widen the scope of the system. The emphasis of *Chapter 6* is on the purification and structure determination of organic molecules. In this context the chromatography section has been restructured to make it more useful and to prepare the students for laboratory work. *Chapter 7* deals with alkanes, their general methods of preparation and properties. Every effort has been made to avoid

superfluity and wherever possible clear explanation for chemical properties and reactivity has been offered. This trend has been followed in the subsequent chapters.

The next fourteen chapters (*Chapters 8 through 21*) describe alkenes, alkynes, polymers, alicyclic compounds, aromatic hydrocarbons, organic halogen compounds, alcohols and phenols, ethers, thioethers and thiols, aldehydes and ketones, carboxylic acids and their functional derivatives, sulfonic acids and amines. This main body of the text has been the focus of major revision. A new chapter (*Chapter 10*) on natural and synthetic polymers, an important area in Organic Chemistry has been added. The Diels-Alder reaction, the Friedel-Crafts reaction, aromaticity, hydroboration, analysis of oils and fats and the various condensation reactions have been extensively revised. Besides the elucidation of reaction mechanisms, emphasis has been laid on the synthetic applications of the important reactions. Synthetic uses of esters of special interest such as acetoacetic ester, malonic ester and cyanoacetic ester have been presented with appropriate examples. The organometallic compounds including the Grignard reagents have been discussed in a separate chapter (*Chapter 22*). The second edition, like the first, provides a transition from the carbocyclic to the heterocyclic compounds (*Chapter 23*). The last four chapters (*Chapters 24 to 27*) discuss the chemistry of compounds of biological and medicinal significance.

New problems have been added to each chapter, some of which are useful for routine drill while some are expected to provide challenge to the students. The students are advised to solve the problems independently. Brief answers to the questions are given at the end of the book.

The revision of the book has been a difficult exercise in self-restraint. It is, however, a result of a selective process of topic addition and modification. At the same time I have made every effort to preserve the carefully developed expositions for which the *first edition* was so widely acclaimed.

I am indebted to many colleagues and friends who have helped me during the revision of this book. Valuable comments among others by Professors P. Bajaj, A.S.N. Murthy and Dr. P.S. Pandey (Indian Institute of Technology, Delhi); Professor S.V. Kessar (Punjab University, Chandigarh); Professor Harjit Singh (Guru Nanak Dev University, Amritsar); Professor K.C. Joshi (Rajasthan University, Jaipur); Professor B.C. Verma (Himachal Pradesh University, Shimla); Professor S.K. Srivastava (Roorkee University, Roorkee); Drs. K.M. Pant and B. Prakash (N.C.E.R.T., New Delhi); are gratefully acknowledged.

My special thanks are due to my wife Kusum Bansal for her remarkable patience and unflagging enthusiasm during the period I took in working on the second edition. I also appreciate the assistance of my sons Robin and Rajiv in making the index. In addition, I wish to thank the staff at Wiley Eastern who helped bring this text to fruition.

Raj K. BANSAL

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Introduction

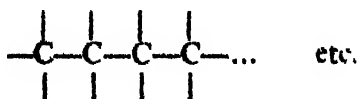
The subject of organic chemistry pertains to a systematic study of the compounds of carbon. The organic compounds were initially considered to be derived from animal and vegetable sources. These compounds were recognized to be different and more complex than those obtained from the mineral world, i.e. the inorganic compounds. All organic compounds contain carbon; most of them contain hydrogen; many contain oxygen; some contain nitrogen; while a few contain elements such as sulfur, phosphorus, arsenic, chlorine, bromine, iodine, etc.

Earlier it was believed that a *vital force* present only in living organisms could produce the organic compounds. This came to be known as the *vital force theory*. As a result, no attempt was made to prepare organic compounds in the laboratory till F. Wohler, a German chemist, in 1826 synthesized urea by heating together ammonium chloride and silver cyanate.



Urea is a well known organic compound that has been isolated from urine and moreover, its synthesis is important in the chemical industry because of its use in plastics and agriculture. A few years later Kolbe synthesized acetic acid. These brilliant successes gave a blow to the erstwhile *vital force theory* and its complete demise occurred around 1850.

A question naturally arises as to why organic chemistry should be treated as a separate branch of chemistry. This question may probably be answered by the unique position enjoyed by the carbon atom in the periodic table of elements. Carbon lies in the 4th group of the second period and possesses an atomic number of six. It has four valence electrons and requires a total of eight electrons to attain the stable rare gas configuration corresponding to neon. Furthermore, because of its central position, it is neither strongly electropositive nor strongly electronegative. As a matter of fact carbon forms bonds with other elements by sharing of electrons rather than by complete gain or loss. Carbon atoms can share electron with atoms of their own kind more easily than any other elements to form long chains.



Because of this reason carbon atom is capable of forming a large number of compounds.

There is a great deal of interest these days in the preparation of new compounds. Numerous reagents and techniques are available in the arsenal of an organic chemist for this purpose. The purity and structure of organic compounds are established by sophisticated analytical methods available currently. The number of organic compounds are estimated to be close to two million. Besides, there had been two important phenomena in organic chemistry, namely, *isomerism* and *homology* which explained the existence of a large variety of carbon compounds. The early chemists classified organic chemistry into aliphatic and aromatic.

Organic compounds and the chemical industry affects our daily life in a number of ways. Nature abounds in organic compounds of nearly every conceivable structural class, the study of which is very fascinating. The living organisms, bacteria, fungi, plants and animals are the sites of complex synthetic activities. Organic chemistry is associated with our food, clothing, furniture, medicines, etc. There are two chief sources of organic compounds, namely, petroleum and coal tar besides, of course, the plant and animal kingdom. Coal tar provides a rich source of industrial organic chemicals. Petroleum is a complex mixture of hydrocarbons, and of some nitrogen and sulfur derivatives as well. In the living organism, the organic compounds are synthesized by a process termed as *biosynthesis*. Important compounds obtained from the above sources are drugs, perfumes, sugar and rubber (plants), oils, fats and proteins (animals), insecticides, dyes, and explosives (coal), and lubricants, solvents, refrigerants and fuels (petroleum).

Finally, the study of organic chemistry is important to an individual depending on the type of profession he wishes to adopt. An individual may like to devote his lifetime to the cause of chemistry or may plan to enter medicine or pharmacy or chemical engineering. All these branches of science require an adequate background of organic chemistry. A sound knowledge of organic chemistry is essential to study *biochemistry* which deals with the reactions taking place in the living organisms. Organic chemistry plays a significant role in the life of engineers because most of the reactions that they encounter are indeed organic reactions.

Organic chemistry is a creative and fascinating subject. The thrill of it lies in knowing it. An introductory knowledge is essential for everybody in this technical age.

Electron and the Chemical Bonding

Progress in any discipline comes slowly and often requires the efforts of many workers. One is sometimes inspired by the findings of the others, which result in a viable solution to the problem. This is true in particular, of the modern concept of atomic structure. Matter was considered to be composed of atoms, which in turn were thought to be the smallest particles possible. Such an idea traces back to the classical times and was based mainly on the philosophical speculations of the Greek philosophers. But as scientific thought advanced and experimentation became possible, this view concerning the atom proved to be quite inadequate to explain the observed facts.

Historically speaking, the development of the modern atomic theory commenced with the work of Dalton (1803) in the form of several postulates. One of the postulates stated that atoms could not be sub-divided or converted into one another. Important contributions were made by various chemists and finally Thomson (1897) actually discovered electrons by his brilliant discharge tube experiments. This opened a new era in unfurling the structure of the atom. Rutherford (1911) presented a picture of the structure of the atom according to which the negatively charged particles designated electrons revolve around a positive nucleus in analogy with the solar system. Bohr (1913) announced the quantum theory of the atom and gave a mathematical treatment for the simple hydrogen atom. de Broglie (1923) postulated the wave nature of electrons analogous to light waves and finally Schrödinger's (1926) mathematical equation called the "*wave equation*" summed up the present concept of the electron.

1.1 ATOMIC ORBITALS

An electronic interpretation of chemical bond formation was proposed by Lewis in which the elements tend to gain or lose electrons in such a way as to acquire a noble gas configuration. The model is undoubtedly useful for many purposes but electrons, as we know now, do not stay still in one position. The modern discussion on chemical bonding is, therefore, related to wave functions or orbitals. From a consideration of wave mechanics a basic concept arises called the *Heisenberg uncertainty principle* which states

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that it is impossible to specify the position and velocity of an electron simultaneously. In other words, if we know the position of an electron accurately its velocity at that moment will be uncertain. We, therefore, consider the electron as having a certain probability of being located at any given instant in space. Such a location, called an *orbital* may be visualized as a charged cloud being dense at places where such a probability is high and less dense where the probability is low.

A wave equation can be written for any atom or molecule and the solutions of the equation are termed as *wave functions* denoted by ψ . These wave functions give information about the orbitals occupied by the electrons of a system and the square of the wave function (ψ^2) for a particular location (x, y, z) refers to the probability of finding an electron at that particular location in space. If ψ^2 is large in a unit volume of space, the probability of finding an electron in that volume is great; in other words, the electron probability density is large and vice versa.

An orbital is simply that region in space in which the electron is likely to be found. The solution of the wave equation gives the probability density of the electron. Let us consider a hydrogen atom in the ground state. This atom consists of a positively charged nucleus and one extranuclear electron. The probability that the electron is at a distance r from the nucleus is plotted against r (Fig. 1.1). Of all the possible locations of the electron of

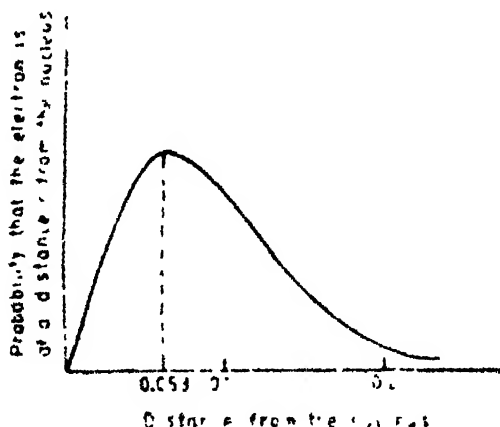


Fig. 1.1 A curve showing the radial electron probability *versus* distance (r) from the nucleus for hydrogen atom.

the hydrogen atom, the distance 0.53 \AA from the nucleus has the highest probability. This implies that the electronic charge cloud corresponding to the hydrogen atom in its lowest energy state ($1s$) occupies the space within a radius of 1 \AA from the nucleus and is spherically symmetrical. Also the value ψ_{1s}^2 (for hydrogen) varies with distance r from the nucleus.

According to the wave mechanical theory of the atom, each solution to

the wave equation is characterized by a set of definite values for four numbers, called the *quantum numbers*, these are often represented by n , l , m and s . These numbers can have the following values:

$$n = 1, 2, 3, 4, \dots, \text{any integer}$$

$$l = 0, 1, 2, 3, 4, \dots, n - 1$$

$$m = +l, (l-1), (l-2), \dots, 0, \dots, (-l+2), (-l+1),$$

$$m = +l, (l-1), (l-2), \dots, 0, \dots, -l$$

$$s = +\frac{1}{2}, -\frac{1}{2}$$

The number n is called the principal quantum number and it represents the energy of an electron in an orbit. The orbit of lowest energy has $n = 1$. An electron in this orbit is in its *ground state*. The next energy level has quantum number 2 and so on.

The number l is known as the angular momentum quantum number and represents the angular momentum of the electron. It is given positive and integral values.

The wave equation leads to a third quantum number m , the *magnetic quantum number*. Since the magnetism is due to the angular momentum, it is expected that value of m will depend on n . It tells about the shape of the orbital.

Finally the fourth number is called the *spin quantum number* s . It has only two values and represents the spin of an electron on its own axis which can be either clockwise or anticlockwise, relative to the orbital of the electron.

1.1.1 Shapes of Atomic Orbitals

The atomic orbitals ($1s$, $2s$ and three $2p$ orbitals) occupy definite regions in space. Both the $1s$ and $2s$ orbitals are spherically symmetrical (Fig. 1.2) about the nucleus. The probability of finding an electron decreases with the increase in distance from the nucleus. Evidently the greater probability is near the nucleus. The sign of the wave function ψ , is positive over the entire $1s$ orbital. The $1s$ and $2s$ orbitals differ primarily in size, the latter being slightly larger. The $2s$ orbital, in addition, contains a nodal surface, i.e. an area where $\psi = 0$.

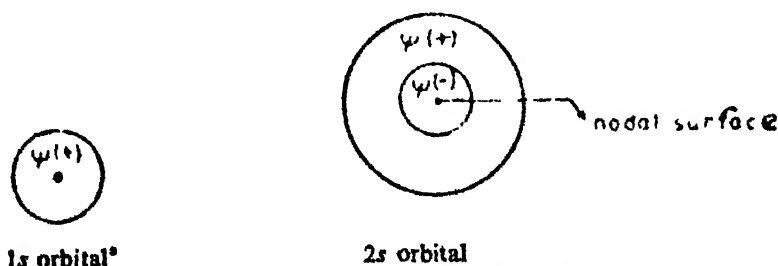


Fig. 1.2 Charge distribution for an electron in an s orbital.

The p -orbitals are three in number, i.e. p_x , p_y and p_z and differ from one another in their spatial orientation. They do not have a spherical symmetry and instead are composed of two lobes that do not touch each other (Fig. 1.3). This point is a place of zero electron density and is known as the *nodal plane*. The sign of the wave function ψ_{2p} is positive in one lobe and negative in the other. The three p -orbitals are arranged in space so that their axes are mutually perpendicular. These are degenerate, i.e. equal in energy.

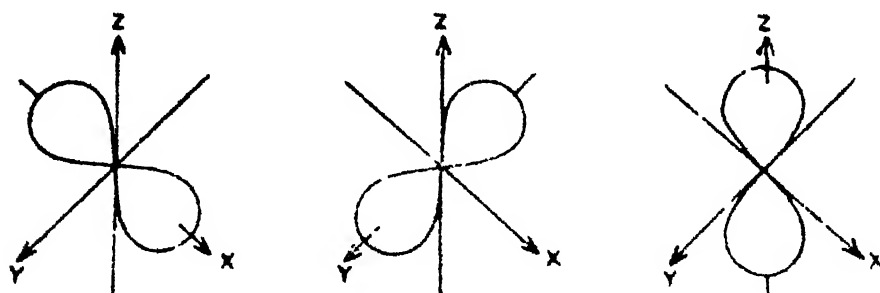


Fig. 1.3 Charge distribution for electron in three p -orbitals

The d -orbitals are five in numbers, more complicated because they differ in shape as well as in orientation. The probability distribution is given in Fig. 1.4.

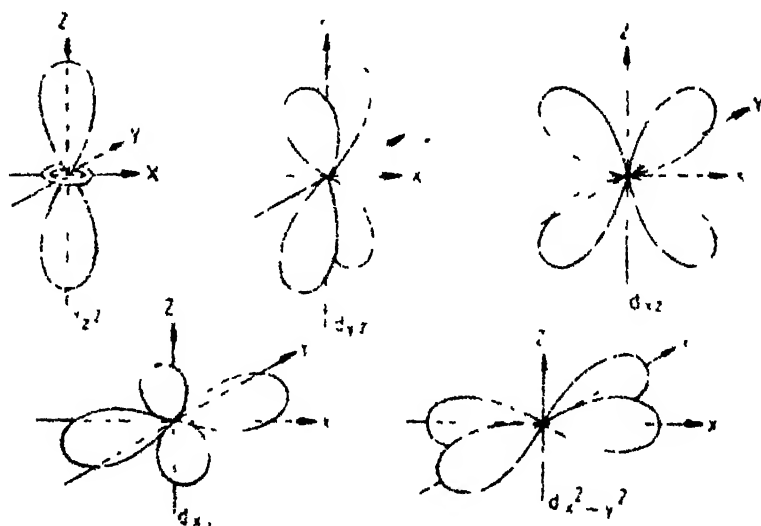
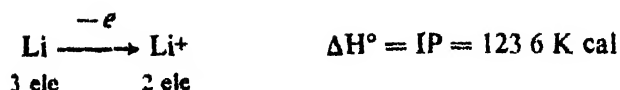


Fig. 1.4 Charge distribution for electrons in d -orbitals

The energy required in removing an electron from an atom is known as *ionization potential (IP)*. The first ionization potential is the energy required to remove the least tightly bound electron from the atom.



The ion so produced has the electronic configuration of the next lower noble gas. Li^+ has the same electronic configuration as helium. The elements on the left side of the periodic table have relatively low ionization potential and are termed as *electropositive*.

The energy evolved when an electron is gained by an atom is known as the *electron affinity* (EA).

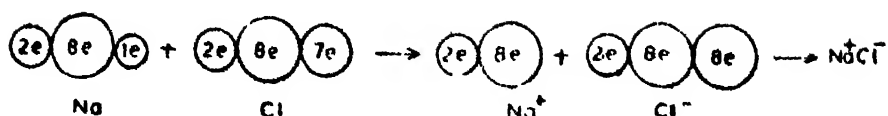


The ion so produced has the stable electronic configuration of the next higher noble gas. In this case it is the same as that of neon. Such elements are termed as *electronegative*.

1.2 CHEMICAL BOND FORMATION

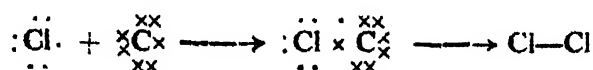
A consideration of chemical combination of atoms and the forces that hold them together can be taken up. The number of electrons in the outermost shell of an element are called the valence electrons and the term *valence* or *valency* may be thought of in terms of a certain combining power. It was recognized earlier that chemical properties of elements depend on the arrangement of their electrons and that the inert gases possess stable configurations. Lewis proposed the *octet theory* according to which, atoms linked by chemical bonds achieve a stable octet of electrons in their outermost shell, and is called the 'rule of eight.'

In the formation of an *ionic bond*, an electron is completely transferred from one atom to another of a different element forming charged particles called *ions*. During this transfer each atom acquires a stable octet or eight electrons analogous to inert gas elements since it is known that such configurations are of exceptional stability. Such bonds are formed between highly *electronegative*, i.e. electron-attracting and highly *electropositive*, i.e. electron-donating elements. The alkali metals of the periodic table have relatively low ionization potential, i.e. can lose electrons easily and are thus described as being *electropositive*. The halogens, on the other hand, can readily gain electrons; such elements are termed as *electronegative*. Thus in bond formation between sodium and chlorine atoms, the latter can either relinquish seven electrons or gain one electron and become a chloride ion. The former process is energetically difficult. The sodium atom loses an electron readily and becomes a sodium ion. This can be depicted as follows:

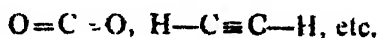


The resulting ions exert an electrostatic attraction and enter into a bond formation. The bond so formed is called the *ionic* or *electrovalent bond* so common in inorganic chemistry, potassium chloride, magnesium oxide, sodium hydroxide, etc. contain ionic bonds. The ionic bond is non-directional because ions radiate a spherically symmetrical positive or negative field.

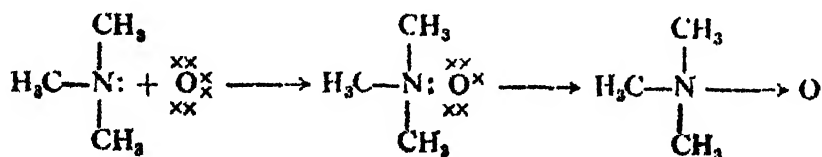
Lewis explained the formation of a *covalent bond* by sharing rather than by transfer of electrons. Two chlorine atoms, for instance, combine in such a way that a pair of electrons is shared by both the chlorine atoms as shown below :



The symbols used to describe such systems are called *Lewis structures*. Molecules like bromine, methane, hydrogen chloride, carbon tetrachloride etc. are examples of compounds containing covalent bonds. A covalent bond can be either polar or non-polar depending on the electronegativities of the two linked atoms. Larger the difference in electronegativity of the bonded atoms, more polar is the bond. If more than one pair of electrons is shared by the atoms then multiple covalent bonds are formed, for example,

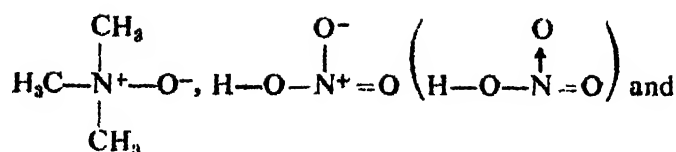


There is yet another way of octet formation. In this case the bonding electrons are provided by one of the two partners and then shared jointly. For example, consider the amine oxide molecule which is formed by combining trimethylamine with oxygen.



The nitrogen atom of the amine provides the two electrons and is referred to as the *donor* atom and such a pair is called the *lone pair*. The oxygen atom which accepts the electron pair is known as the *acceptor*. This type of bond is called the *coordinate* or *dative bond*, and is expressed by an arrow (\rightarrow) pointing towards the acceptor. The formula may also be described in a

dipolar form as follows :



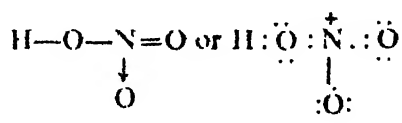
Many inorganic salts, in particular, contain more than one type of bond between their atoms. For instance, KCN contains both ionic and covalent bonds; and $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ has ionic, covalent and dative bonds

1.2.1 Formal Charge on an Atom

Formal charge may be described as the excess or lack of electrons at an atom in the molecules as compared to the free atom. In order to calculate the formal charge on an atom, it is assumed that the atom has possession of half the shared electrons. The following expression can then be employed to calculate formal charge on an atom :

Formal Charge Valence electrons of the isolated atom—(unshared electrons + $\frac{1}{2}$ shared electrons)

The valence electrons are the number of electrons in terms of its position in the periodic table, for *carbon* it is 4, *nitrogen* 5, *oxygen* 6, *halogens* 7, *sulfur* 8. In nitric acid, for instance, nitrogen has no unshared electrons but eight shared electrons, therefore, the formal charge on nitrogen is equal to

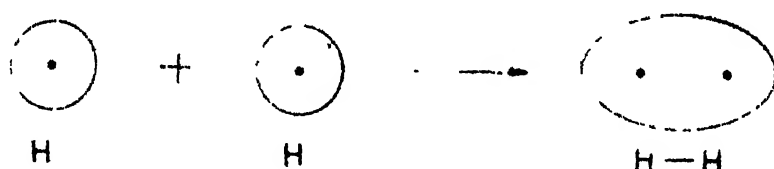


$[5 - (0 + 8/2)]$ 1, nitrogen thus has one formal charge and oxygen atom similarly has a formal charge equal to $[6 - (6 + 2/2)] = -1$. The atoms in the $\text{H}-\text{C}\equiv\text{N}$ molecule have no formal charge, whereas in carbon monoxide ($:\text{C}:::\text{O}:$), the carbon has a single negative formal charge and oxygen a single positive formal charge. In the nitronium ion ($\text{O}=\text{N}^+=\text{O}$) oxygen has a zero formal charge but nitrogen has $+1$ formal charge.

1.2.2 Modern Concept of Bond Formation

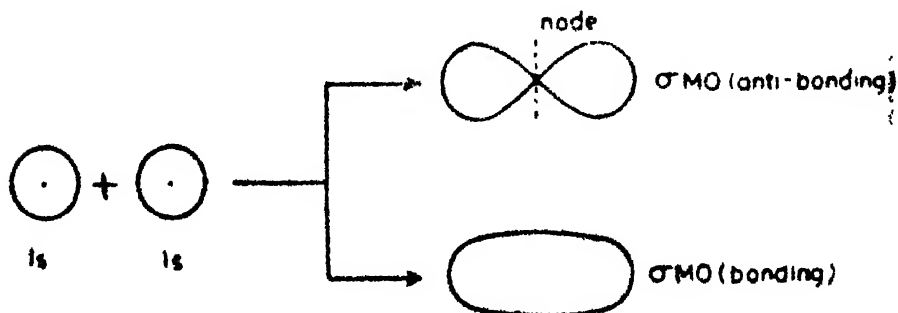
The so-called 'rule of eight' no doubt explains the covalent bond formation in a large number of cases but discrepancies, do occur. For example,

although it is known that BCl_3 is a covalent compound, one finds that there are only six electrons around the boron atom instead of the required eight. It follows that we have to modify our way of explaining a chemical bond formation. This is done in terms of the orbitals, i.e. the bond formation involves the filling of incomplete or empty orbitals of an atom by the electrons of the other. In the $\text{H}-\text{H}$ bond formation, each hydrogen has a single unpaired electron in the $1s$ atomic orbital. The electron charged clouds approach each other and the atomic orbitals combine to form a hydrogen molecule. In the hydrogen molecule, the two electrons remain most of the time between the nuclei holding the molecule together. In wave mechanical terminology, the process is called overlap. The term *overlap* refers to the extent to which atomic orbitals on different atoms share the same region of space to form a molecular orbital. A hydrogen molecule results from the formation of a hydrogen-hydrogen covalent bond, such a process occurring with the pairing of spins denoted as $\uparrow\downarrow$. The orbital so obtained is called the *molecular orbital*. In the formation of a bond, certain amount of energy is released, the hydrogen molecule is thus 104.2 Kcal/mole more stable than each of the hydrogen atoms. The larger the degree of overlap of the atomic orbitals, the greater is the energy of the bond formed.



This new orbital is no longer spherical in shape rather tends to have a higher electron density between the two hydrogen nuclei. The bond so formed is described as a *sigma* (σ) bond.

If we start with two or more atomic orbitals, the same number of new molecular orbitals are formed. In the case of hydrogen, on combination, the two atomic orbitals are split into two new energy states. In terms of molecular orbital theory, the lower energy orbital is a bonding *orbital* and



that of higher energy is the *anti-bonding* orbital. This type of orbital contains a nodal plane. Formally, only orbitals that are not filled or are incomplete participate in orbital overlap.

1.3 BOND DISSOCIATION ENERGIES

When atoms combine to form molecules, energy is released. The molecule has a lower energy than its constituent atoms. For instance, when two hydrogen atoms combine to form a hydrogen molecule, the reaction is exothermic and 104.2 Kcal of heat is evolved per mole of hydrogen produced.



Nevertheless, the atoms are held together by forces which can be estimated. We may define this force as the energy contained between the two atoms and may be termed as bond energy (L) or the heat of formation of the bond. The total energy contained in a molecule is the sum of the bond energies of all the bonds constituting the molecule.

The energy required to break a covalent bond into its fragments is called dissociation energy (D). It is a measure of the strength of a bond. This is an endothermic process. The energy absorbed to break a H—H bond is exactly equal to that evolved in its formation, but ΔH is now positive.



Determination of bond dissociation energy is an experimental process and is usually calculated from thermochemical data. Bond dissociation energy values for some common bonds are given in Table 1.1. The dissociation energy of a bond increases with the difference in the electronegativities of

Table 1.1. Single Bond Dissociation Energies (Kcal/mole)

Bond	Bond Dissociation Energy	Bond	Bond Dissociation Energy
H—H	104.2	H—O	102.4
D—D	106	I—I	46.1
C—C	83.1	H ₃ C—H	104
O—C	31.2	C—F	105.4
F—F	36.6	C—Cl	83.5
Cl—Cl	58.0	C—Br	70.0
Br—Br	46	C—I	56
F—P	38	Na—Cl	98.1

the bonded atoms. Furthermore, the shorter the bond, the stronger is the bond.

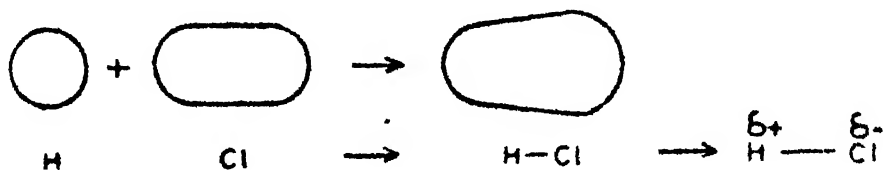
1.4 ELECTRONEGATIVITY AND BOND POLARITY

Electronegativity is defined as the tendency of an atom to attract electrons. The elements with high electronegativity are up and to the right of the periodic table, i.e. going across the top row, the electronegativity increases in the order $\text{Li} < \text{C} < \text{N} < \text{O} < \text{F}$. The electronegativity of the halogen atoms decreases in the sequence $\text{F} > \text{Cl} > \text{Br}$, i.e. fluorine has the highest electronegativity.

The relative electronegativities of the electron commonly encountered in organic molecules are as follows :



In this series hydrogen is least electronegative. The more electronegative an element, the greater will be its hold on the electrons. In a covalent bond the sharing of electrons between the atoms need not be equal except in the case of two identical atoms. Unlike atoms bonded together have different electronegativities. This difference in electronegativity gives a partial negative (δ^-) charge to the more electronegative atom and a partial positive (δ^+) charge to the second atom, as shown for HCl molecule.



A greater share of the pair of electrons is held by the chlorine atom and as a result the molecular orbital is unsymmetrical, such a bond is termed as a *polar covalent bond*. Extreme differences in electronegativity cause the atoms to form an ionic bond ($\text{Li}^+ \text{F}^-$). If the bonded atoms, on the other hand, are identical such as that in Cl_2 molecule, then the bond is considered *non-polar*. Electronegativity can be measured on a relative scale. Accordingly Pauling proposed a scale on the basis of measurements of bond dissociation energies.

1.5 HYBRIDIZATION AND SHAPES OF MOLECULES

It has been observed that the number of covalent bonds formed by an atom is equal to the number of electrons in its outermost shell. However, certain atoms such as carbon, boron and beryllium do not obey this generalization. They rather form more covalent bonds than might be

predicted. The most logical explanation of this fact is that hybrid covalent bonds exist in compounds of C, B and Be. To understand this let us consider the electronic configuration of these three elements.

	1s	2s	2p _x	2p _y	2p _z
C (ground state)	↑ ↓	↑ ↓	↑	↑	
B (ground state)	↑ ↓	↑ ↓	↑		
Be (ground state)	↑ ↓	↑ ↓			

An examination of these electronic configuration indicates that carbon should be divalent, boron monovalent while beryllium should not form any bond at all. In practice, however, this is not so, because carbon forms four covalent bonds, boron three and beryllium two. Therefore, to explain the tetravalency of carbon it is assumed that one electron from the 2s orbital is promoted to the vacant p_x orbital as shown below :

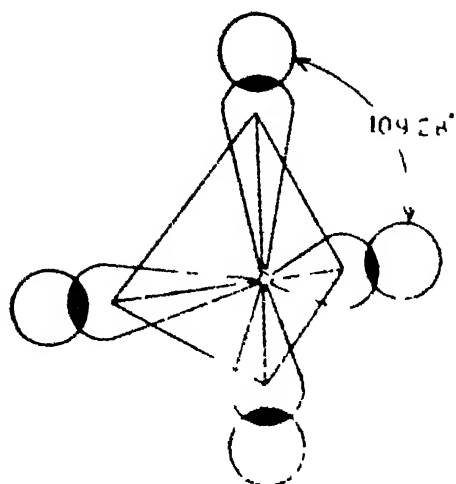
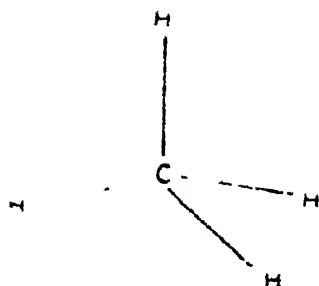
	1s	2s	2p _x	2p _y	2p _z
C (excited state)	↑ ↓	↑	↑	↑	↑

Thus by mixing the orbitals four new equivalent orbitals containing one electron each are formed. These are hybridized orbitals and the process of mixing of orbitals of different energy levels is called as *hybridization*. The new orbitals are written as $4sp^3$, and have 25% s character 75% p character. This concept was developed by L. Pauling an American chemist. The four hybridized orbitals point towards the four corners of a tetrahedron. The shape of an sp^3 orbital is shown below and it consists of two lobes, one large and one small. For the sake of clarity the smaller lobe is often omitted. It is only with the large lobe that any appreciable overlap takes place. The four unfilled hybrid orbitals can overlap with the unfilled orbitals of hydrogen to form the four tetrahedrally equivalent C—H covalent bonds of methane as depicted below :



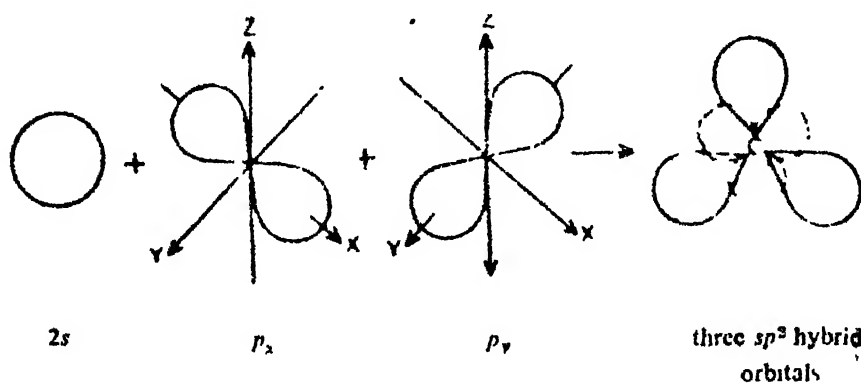
An sp^3 hybridized orbital

The methane molecule is tetrahedral because the four hydrogen atoms and the four pairs of bonding electrons are as far apart as possible from one another but still close enough to form the covalent bonds. The sp^3 hybridization is typical for carbon atoms in saturated compounds.

 sp^3 hybrid orbitals of methane

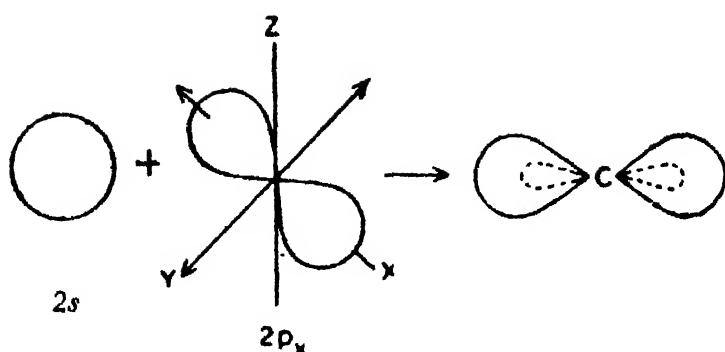
Methane molecule

Two other types of hybridization are assumed in compounds containing multiple bonds such as in ethylenes and acetylenes. In ethylene a different mode of hybridization is proposed, i.e. one $2s$ orbital and only two $2p$ orbitals electrons are permitted to mix giving rise to three equivalent orbitals as shown below. Such a carbon atom is said to be sp^2 hybridized.



The sp^2 hybridized orbitals are planar and the lobes subtend an angle of 120° . The sp^2 orbitals have one part, the character of an s orbital and two parts, the character of a p orbital.

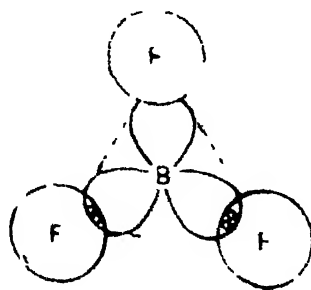
The second is the sp hybridization which is formed by the mixing of one s and one p orbitals. The sp hybridized orbitals are oriented at an angle of 180° , i.e. they are linear. This type of hybridization is characteristic of compounds containing triple bonds and also of cumulenes.



Similarly in boron one $2s$ electron is promoted to the vacant $2p_x$ orbital, as depicted below:

	$1s$	$2s$	$2p_x$	$2p_y$	$2p_z$
B (excited state)	$\uparrow \downarrow$	\uparrow	\uparrow	\uparrow	

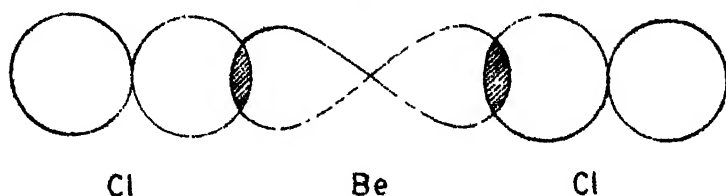
Now mixing the three orbitals results in three equivalent hybridized orbitals. In this case they are sp^2 hybridized orbitals. The bonding formed by the overlap of sp^2 hybridized orbitals with p -orbitals of fluorine in BF_3 is shown below:



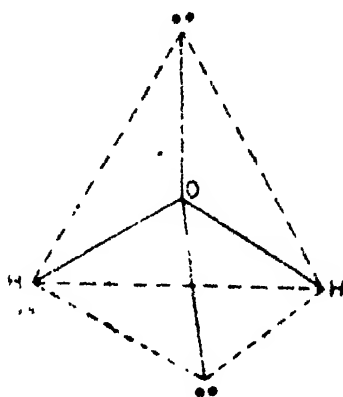
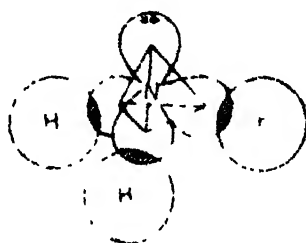
The three atoms form a triangle about the central atom and the shape is described as *trigonal planar*. The angle between the bonds is 120° .

In beryllium the $2s$ and $2p_x$ orbitals hybridize in the excited state. The result is two sp hybridized orbitals. The orbital representation for BeCl_2 is as follows :

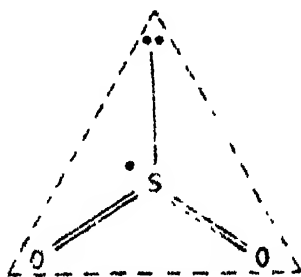
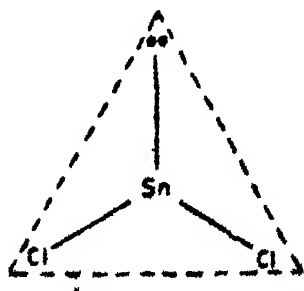
Because the sp bonds are linear, the bond angle is 120° . Some other examples of linear molecules are BeF_2 , BeH_2 , HgCl_2 .



Ammonia, ammonium ion, water, silicon fluoride, methane are tetrahedral. In ammonia the bond angle is 106° , in ammonium ion 109.8° (same as in methane) and in water 104.5° .



The molecules of stannous chloride (SnCl_2), sulfur dioxide (SO_2), nitrite ion and ethylene are sp^2 hybridized.



1.6 BOND ANGLE

The strongest bonds will be formed if the atoms approach in such a manner that there is a maximum overlap between the atomic orbitals. Since orbitals have different shapes, therefore, a covalent bond will have a preferred direction.

A covalent bond is thus oriented in space with respect to one another. From the previous section we have noticed that the s -orbital is spherically symmetrical and overlaps another s -orbital in all directions. The p -orbitals, on the other hand, are directed at right angles to each other, i.e. they possess directional properties. Furthermore, the sp^3 hybrid orbitals of carbon have an angle of 109.28° , sp^2 120° and sp 180° with respect to one another. Therefore, bonds exhibiting these different types of hybridization show different bond angles. Therefore, in addition to bond energy and bond distance, this is another property of bonds. The bond angles are determined by the atomic orbitals involved in bond formation. Deviations, however, do occur in many cases. In water, for instance, the H—O—H bond angle is 104.27° . The H—O—H angle is close to the tetrahedral angle. The bonds in water are thus in an sp^3 hybridized state. A tetrahedral structure for water can be written if we place the two non-bonding electron pairs at the corners of a tetrahedron.

1.7 BOND LENGTH

The bond length between two bonded atoms A—A can be described as their internuclear distance. This distance is usually very small and is expressed in angstrom units (\AA). This type of information has been obtained with a high degree of accuracy by electron diffraction and X-ray diffraction methods. The magnitude of length depends upon a number of factors such as orbital hybridization, resonance effects etc. These factors usually tend to shorten the bond distance. Table 1.2 records the bond lengths of some carbon compounds.

Table 1.2 Normal Bond Lengths

Bond	Bond Length (\AA)	Bond	Bond Length (\AA)
C—H	1.07	$\begin{array}{c} \\ \text{=C—H} \end{array}$	1.07
O—H	0.96	$\equiv\text{C—H}$	1.05
C—C	1.54	—C—C—	1.35
C—Cl	1.76	$\text{—C}\equiv\text{C—}$	1.20
C—Br	1.94	$\begin{array}{c} \diagdown \\ \text{C} \quad \text{O} \\ \diagup \end{array}$	1.22
C—I	2.14	C—N—	1.16

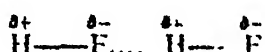
It is clear from the Table that a carbon-carbon multiple bond is shorter than a carbon-carbon single bond. This difference is attributed to the change in the hybridization of the carbon atom. With greater electron density between the two carbon nuclei in the multiple bonds, the two nuclei are drawn closer together.

The covalent bond lengths are nearly constant in a given series of related atoms and this constancy of bond lengths reflects the fact that the properties of individual bonds are, to a good approximation, independent of the remainder of the molecule.

1.8 THE HYDROGEN BOND

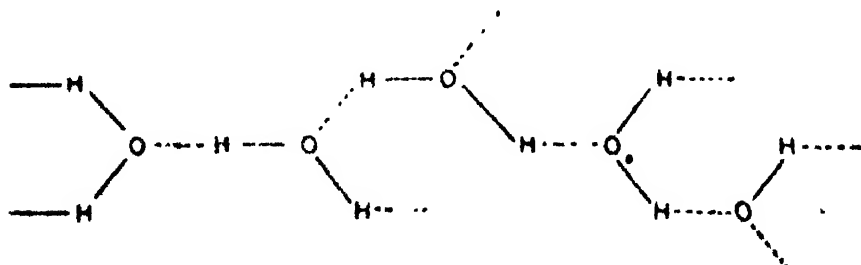
The attraction between a hydrogen atom in one molecule and an electronegative atom in another molecule is called a *hydrogen bond*. Let us consider the hydrogen fluoride molecule. The bond in it being covalent polar can

be written as $\overset{\delta+}{\text{H}}-\overset{\delta-}{\text{F}}$. If another HF molecule comes closer then there will be an attraction between the negative end of one molecule and the positive end of the other as shown below:



There is a bond formation between F and H atoms. In other words, when a hydrogen atom is flanked by two electronegative atoms a hydrogen bond formation takes place. The bond results from electrostatic attraction. It is represented by a dotted line and is very weak but strong enough to appreciably effect properties of molecules. Hydrogen bond occurs in compounds like alcohols, water, hydrogen fluoride, ammonia, etc. There are two types of hydrogen bonds, namely *intermolecular* (between two or more molecules) and *intramolecular* (within the same molecule). Both types effect the properties of molecules. This point can be illustrated by considering some examples.

Intermolecular H-Bond. As stated earlier intermolecular H-bond occurs between two or molecules of the same or different types. Water and hydrogen sulfide are hydrides of elements in the sixth group of the periodic table. The boiling point of H_2S is 40°C while that of water is

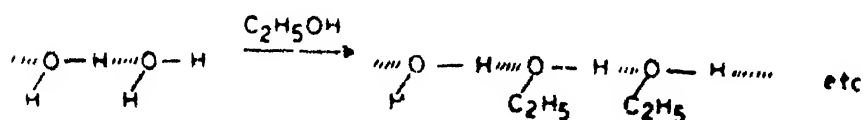


much higher, 100°C. This increase in boiling point of water is explained on the basis that association of water molecules takes place in the liquid state. The hydrogen bonds link the water molecules together to form a huge molecular aggregate. Extra energy is thus required to break the hydrogen bonds, which raise its boiling point. Hydrogen sulfide, on the other hand, lacks this association.

The bonds in water molecule are inclined at approximately the tetrahedral angle. Water molecules are associated in liquid water. In ice the arrangement of molecules is similar but the regularity extends throughout the whole structure. The structure spaces the molecules further apart than they are in liquid water. Ice thus occupies more space than the original liquid. This explains why water expands on freezing.

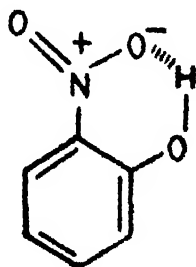
Ethanol (78.3°C) boils higher than the isomeric compound dimethyl ether (-24°C) and phenol (182°C) boils higher than toluene (110.6°C).

For a substance to be soluble in water, it should be able to associate with water. Both ethanol and methanol are miscible with water in all proportions because of coordination with water.

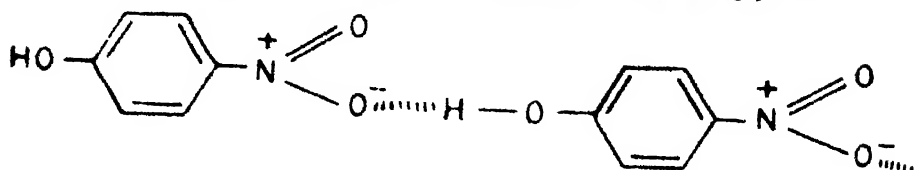


Ethers, higher alcohols and hydrocarbons are not soluble in water because they cannot associate with water.

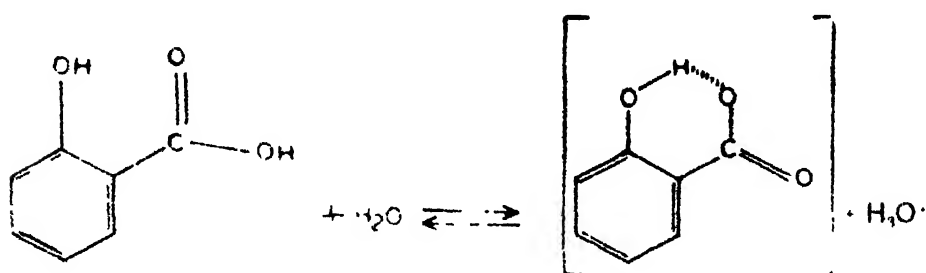
Intramolecular H-Bond: A large number of molecules are capable of forming intramolecular hydrogen bond between two groups present in the same molecule. This type of association also alters the properties of molecules. Phenol, for instance, on nitration affords a mixture of *o*- and *p*-nitrophenols. The isomers can be separated by steam distillation as the *o*-isomer distils over while the *p*-isomer remaining in the flask can be recrystallized. This difference in boiling point of the two isomers has been explained on the occurrence of intramolecular hydrogen bonding in *o*-nitrophenol and intermolecular hydrogen bonding in the *p*-isomer.



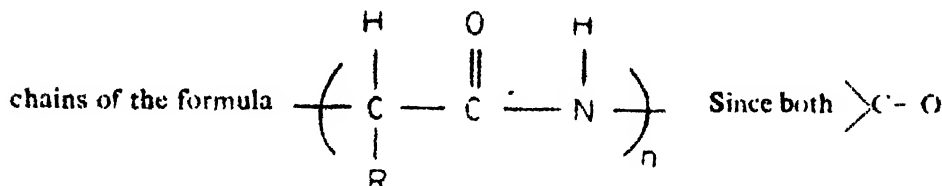
p-Nitrophenol because of hydrogen bond formation becomes a closely knit large aggregate which causes the increase in its boiling point.



Occurrence of intramolecular hydrogen bond seems to influence the acidity of certain carboxylic acids. Salicylic acid, for instance, is 35 times more stronger than *p*-hydroxybenzoic acid. The salicylate ion is stabilized by intramolecular hydrogen bond formation.



Hydrogen bond is important in proteins also. Proteins contain long



and >N-H bonds are polar, intramolecular hydrogen bond formation can between them. Several such hydrogen bonds are present in a single protein molecule, and it is held in a three-dimensional arrangement.

1.9 POLAR MOLECULES AND DIPOLE MOMENT

In a non-polar bond the electric charge is equally distributed between the identical atoms. Examples are those of N_2 , Cl_2 , Br_2 , etc. If there is a charge displacement towards the more electronegative atom, the bond is polar. As we have seen before this is the case with HCl and the molecule is polar. When the centers of positive and negative charges do not coincide they constitute a dipole and the molecule is said to possess a dipole moment. It is defined as the product of the electrical charge (q) and the distance (d) between them and is represented by μ . It is expressed in Debye units (D). Dipole moments of some common compounds are listed in Table 1.3.

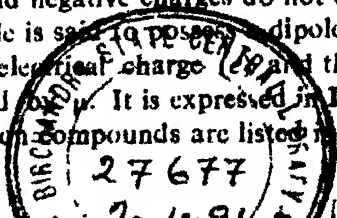
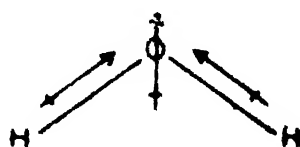


Table 1.3. Dipole Moments of Some Common Compounds

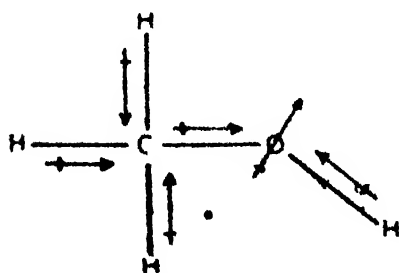
Compound	Dipole Moment (μ_D)	Compound	Dipole Moment (μ_D)
N_2	0	CH_3Cl	1.83
Cl_2	0	CH_3Br	1.79
Br_2	0	CH_3I	1.64
H_2S	0.93	CH_3OH	1.69
$C_2H_5OC_2H_5$	1.32	C_2H_5OH	1.74
HCl	1.84	NH_3	1.47
CH_3I	1.03	CCl_4	0

Dipole moment is a vector quantity, i.e. it has both direction and magnitude. The net dipole moment is the vector sum of the dipole moments of the individual bonds. This point can be illustrated with the following examples.

In water the O—H bonds are polar because of the difference in the electronegativity of oxygen and hydrogen. If the bond angle had been 180° , then the two bond moments would have cancelled and the net dipole moment would be zero. Actually the angle is approximately 104° , therefore, water has a resultant molecular dipole. Similarly methanol has a net dipole moment because the H—O—C angle is about 107° and oxygen is more electronegative than either carbon or hydrogen.

Bond dipoles in H_2O 

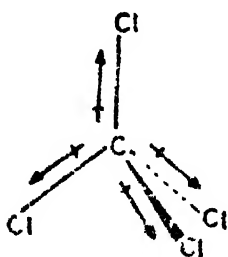
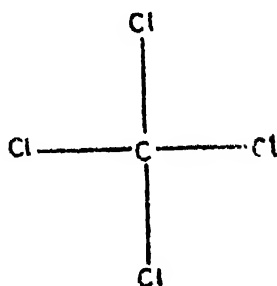
Molecular dipole moment



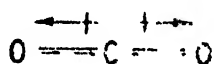
Molecular dipole moment

\rightarrow bond dipole
 $\rightarrow \ominus$ net molecular dipole

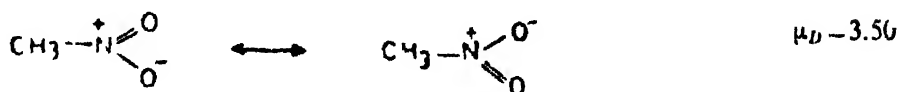
Carbon tetrachloride is a tetrahedral molecule with a bond angle of 109.28° . The four individual C—Cl bonds are polar and the negative end points towards the chlorine atom. The four vectors add up to zero, therefore, carbon tetrachloride has no net dipole moment.

Tetrahedral structure of CCl_4 Planar Structure of CCl_4

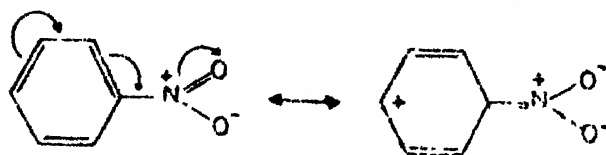
Carbon dioxide molecule is linear and has no net dipole moment. This is because the two component C=O bond moments are opposed and they cancel each other.

Planar structure of CO_2

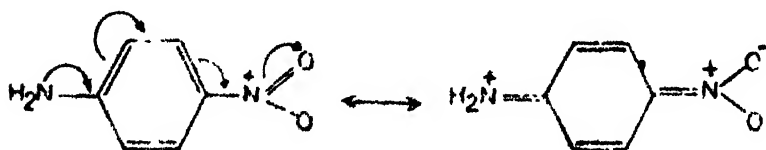
An important factor that influences dipole moment is resonance as it increases the distance between the charges. Let us consider the following three nitro compounds. An examination of the dipole moments indicates that *p*-nitroaniline has the highest value (6.10) because the electrons are transferred from the amino to the nitro group by resonance and this increases the distance of charge separation.



$$\mu_D = 3.50$$



$$\mu_D = 4.95$$



$$\mu_D = 6.10$$

For the same reason CH_3Cl ($\mu_D = 1.87$) has a large dipole moment than CH_3F ($\mu_D = 1.81$) because the $\text{C}-\text{Cl}$ bond is longer though fluorine is more electronegative than chlorine.

The ease with which a dipole may be induced in a molecule is called its *polarizability*. As the number of electrons in a molecule increases its polarizability also increases. Iodine, for instance, has a greater polarizability than bromine.

QUESTIONS

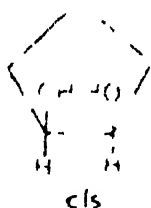
1.1 Write short notes on the following :

Polarity of bonds, bond angle, association, electropositive elements, hydrogen-bond, bond length and dissociation energy.

1.2 Distinguish between *s*-orbital, *p*-orbital, sp^2 and sp^3 hybridized orbitals.

1.3 Why is methane tetrahedral?

1.4 Intramolecular hydrogen-bonding occurs in *cis*-1, 2-cyclopentanediol but not in the *trans*-isomer. Why?

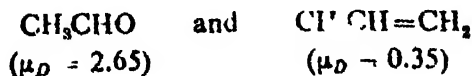


1.5 *o*-Nitrophenol is steam volatile and less soluble than the other isomers.

1.6 Describe the formation and shape of an sp^3 hybridized orbital.

1.7 (a) *p*-Nitroaniline has a dipole moment (6.10 D) greater than the sum of the dipole moments of nitrobenzene (3.95 D) and aniline (1.53 D).

(b) Explain the difference in the dipole moments of the following compounds :



(c) Which of the following two compounds will have a larger dipole moment and why :



1.8 Calculate the formal charges on the atoms indicated in parentheses.

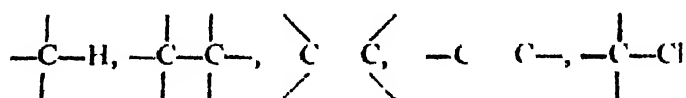


1.9 Indicate the compounds from the following list which have a permanent dipole moment and those which do not :



1.10 The central bond of biacetylene is 1.37\AA whereas a normal C—C bond distance 1.54\AA . How do you account for this difference ?

1.11 How do the bond lengths and bond angles vary in the following cases?



1.12 Explain the following terms .

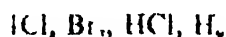
Bond length, bond energy and bond angle.

1.13 Explain what is meant by dipole moment? Name two compounds which show dipole moment and two which do not

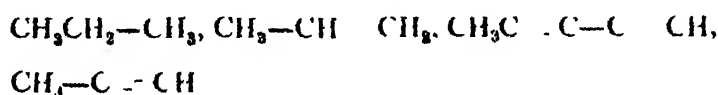
1.14 What are hybridized orbitals? Justify the introduction of the concept of hybridization in certain cases, and give an example of each type

1.15 Why is it necessary to invoke sp^2 hybridization to explain bonding in C_2H_4 ?

1.16 Predict the direction of the dipole moment, if any, in the following molecules :



1.17 Which of the following single bond is shortest in length



1.18 Predict the shape of the following molecules :



1.19 Water has dipole moment but carbon dioxide has not.

1.20 Give an example of an element that undergoes sp hybridization in forming covalent bonds, with other elements. What is the angle between the bonds that result from $s-sp$ overlap of atomic orbitals.

1.21 Why does ice contract when it melts?

2

Classification and Nomenclature of Organic Compounds

A carbon atom has the remarkable capability of forming covalent bonds with elements like H, N, S, O, the halogens, etc. Moreover it can enter into bond formation with other carbon atoms as well. This property has resulted in an almost infinite variety of organic compounds which show vast differences in physical and chemical properties. To systematize and facilitate the study of organic compounds, they have been divided into different classes depending on the type of functional groups present. A *functional group* is defined as the chemically reactive part of the molecule. Thus the carboxyl group ($-\text{COOH}$) is the functional group of a class of organic compounds known as carboxylic acids. The saturated hydrocarbons, in which all the valencies of carbon atoms are satisfied by hydrogen atoms, do not contain a functional group.

Organic compounds have been broadly divided into two types: (a) acyclic (b) cyclic. The first type of compounds is also known as *fatty* or *aliphatic* (from Greek, fat) and they have either *normal* or *branched* structures. The cyclic compounds are either *carbocyclic* ones containing all carbon atoms or *heterocyclic* ones containing other atoms such as N, S or O in ring formation in addition to carbon. The aromatic compounds are a special class of compounds that contain an alternating system of single and double bonds in a six-membered planar ring.

2.1 NAMING OF ORGANIC COMPOUNDS

There are three methods of naming organic compounds.

Trivial names. Trivial names are also called the *common* names and generally refer to the source of the compounds from which they are obtained. A few examples will help illustrate this point. Oxalic acid (oxalis), allyl alcohol (allium), citric acid (citrus), uric acid (urine), etc. have been derived from the sources mentioned in parentheses. Some names refer to distinct properties of the compounds, for example, glucose (Greek, sweet), acrolein (Latin, pungent). More complex substances such as alkaloids, vitamins, terpenes, carbohydrates are also given common names. The common names of different homologous series are recorded in Table 2.3.

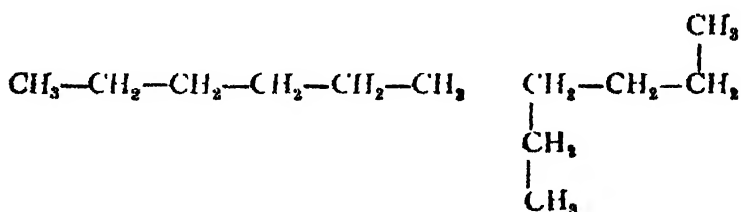
Derived names: Derived names are based on the recognition of certain familiar common names. Thus, in the alcohol series, CH_3OH is called carbinol and $\text{CH}_3\text{CH}_2\text{OH}$, methylcarbinol.

Systematic nomenclature: Because of the multitude of organic compounds known it is impossible to remember the common name of each compound. Therefore, a systematic scheme of naming organic compounds is desirable. The first attempt at such a scheme was made in *Geneva* in 1892. This system is in vogue nowadays and has been recommended by the International Union of Pure and Applied Chemistry and is thus often referred to as *IUPAC nomenclature*.

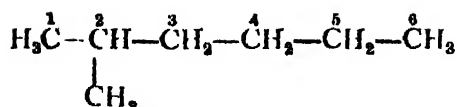
2.1.1 IUPAC Nomenclature

The IUPAC system of nomenclature is applicable to the naming of open-chain compounds. Certain rules have been devised which enable us to translate a structure into a name and *vice versa*. The basic point is to name a compound as a derivative of a straight chain hydrocarbon. This chain of carbon atoms provides the 'root' for the construction of the name of a compound. The rules are stated below:

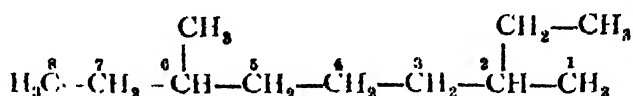
1. The generic name for paraffins or saturated hydrocarbons is alkanes.
2. In a compound to be named, first determine the longest straight chain of carbon atoms. The name of the hydrocarbon corresponding to this chain serves as the basis for the name of the compound. The selection of the chain does not depend upon how it is written. Each of the following two chains consisting of six carbon atoms correspond to hexane.



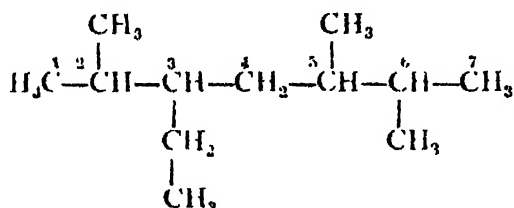
3. To specify the positions of the substituents they are given names and numbers corresponding to their attachment on the straight chain. The name of the alkyl substituent is derived by changing the paraffin hydrocarbon ending *-ane* to *-yl*. The name of several substituents are given in Table 2.1.
4. The carbon chain is numbered commencing at the end nearest the branching if any. This is done to assign the lowest number to the substituent or group present on the chain. The numbering in the following carbon chain starts from left.



5. When the carbon atom bears two similar substituents, their location and number are represented by prefixing *di*-(2), *tri*-(3), *tetra*-(4), etc. before the substituent
6. When two or more groups are located in equivalent positions in the carbon chain, the lower number is assigned to that group which is written first in the name of the compound in the alphabetical order. The numbering in the following chain commences from the right.

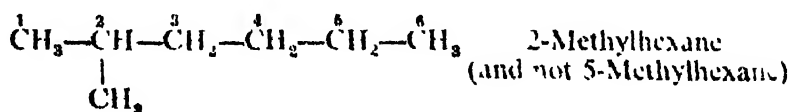


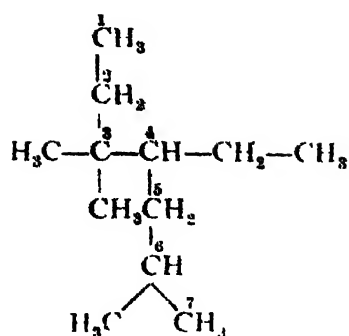
7. In case two chains of equal number of carbon atoms compete for selection as the longest chain, select the one that has greater number of substituents attached to it. The following carbon chain is numbered as shown and then named accordingly. Note that an alternative chain of seven carbon atoms is also available.



8. While writing the name of the compound, place the substituents in an alphabetical order, i.e. ethyl before methyl and bromo before chloro.

The application of these rules may be demonstrated by the following examples:



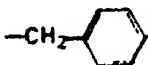
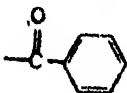
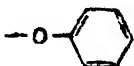
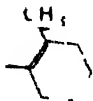





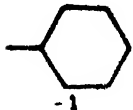




4-Ethyl-3, 3, 6-trimethyl-heptane (see rule 2)

Table 2.1 Names of Organic Substituents

Substituent	Name	Substituent	Name
$-\text{CH}_3$	Methyl	$ \begin{array}{c} \text{CH}_3 \\ \diagup \\ -\text{CH}_2-\text{CH} \\ \diagdown \\ \text{CH}_2 \end{array} $	<i>iso</i> -Butyl
$-\text{C}_2\text{H}_5$	Ethyl	$ \begin{array}{c} \\ \text{CH}_3-\text{CH}-\text{CH}_2-\text{CH}_3 \end{array} $	<i>sec</i> -Butyl
$-\text{CH}_2\text{CH}_2\text{CH}_3$	<i>n</i> -Propyl	$-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$	<i>n</i> -Pentyl
$ \begin{array}{c} \text{CH}_3 \\ \diagup \\ -\text{CH} \\ \diagdown \\ \text{CH}_3 \end{array} $	<i>tert</i> -Propyl	$ \begin{array}{c} \text{CH}_3 \\ \diagup \\ -\text{CH}_2\text{CH}_2-\text{CH} \\ \diagdown \\ \text{CH}_3 \end{array} $	<i>iso</i> -Pentyl
$-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$	<i>n</i> -Butyl	$ \begin{array}{c} \text{CH}_3 \\ \\ -\text{CH}_2-\text{C}-\text{CH}_3 \\ \\ \text{CH}_2 \end{array} $	<i>neo</i> -Pentyl
$-\text{C}\equiv\text{CH}$	Ethynyl	$-\text{CH}_2=\text{CH}-$	Ethylene
$-\text{CH}=\text{CH}_2$	Vinyl	$=\text{CH}_2$	Methylene

$-\text{CH}_2\text{CH}=\text{CH}_2$	Allyl		Ethylidene
	Phenyl	$-\text{OH}$	Hydroxy
	Benzyl	$-\text{OCH}_3$	Methoxy
	Benzoyl		Phenoxy
	<i>o</i> -Tolyl	$-\text{CN}$	Cyano
$-\text{CH}_2\text{Cl}$	Chloromethyl	$-\text{CHO}$	Formyl
$-\text{CH}_2\text{OH}$	Hydroxymethyl		Chloroformyl
	Cyclopropyl		Acetyl
	Cyclobutyl	$-\text{NO}_2$	Nitro
	Cyclopentyl	$-\text{Cl}$	Chloro
	Cyclohexyl	$-\text{Br}$	Bromo
$-\text{I}$	Iodo	$-\text{N}=\text{O}$	Nitroso
$-\text{NHOH}$	Hydroxyamino	$-\text{N}=\text{N}-$	Azo
		$-\text{SCH}_3$	Methylthio

2.1.2 Naming Compounds Containing One Functional Group

The name of a compound containing any one of the functional groups is obtained by adding a *suffix* to the root derived from the name of the hydrocarbon of longest carbon chain. The *suffix* is added in place of the ending *-ane*. The final suffix also controls the numbering as a general rule. The number always precedes the functional group. The various suffixes are set forth in Table 2.2.

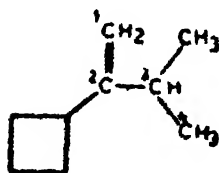
Table 2.2 Suffixes for Functional Groups

Alkenes	<i>-ene</i>	Carboxylic acids	<i>-oic</i>
Acetylenes	<i>-yne</i>	Acid Chlorides	<i>-onylchloride</i>
Alcohols	<i>-ol</i>	Amides	<i>-amide</i>
Aldehydes	<i>-al</i>	Esters	<i>-oate</i>
Ketones	<i>-one</i>	Amines	<i>-amine</i>

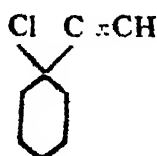
The IUPAC names of lower members of each series are listed in Table 2.3. A few more represented examples are discussed below :



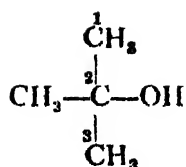
1-Chloroethene



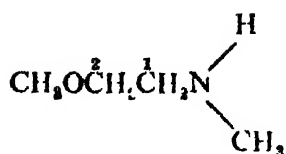
2-Cyclobutyl-3-methyl-1-butene



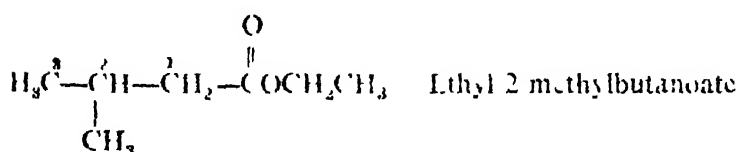
1-Chloro-1-ethynylcyclohexane



2-Methyl-2-propanol



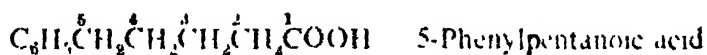
2-Methoxy-N-methylethanamine



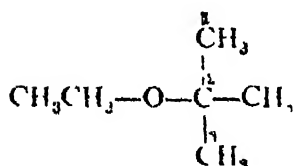
Ethyl 2-methylbutanoate



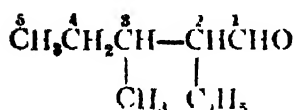
Butanenitrile



5-Phenylpentanoic acid

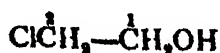


2-Ethoxy-2-methylpropane

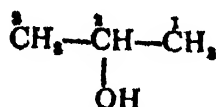


2-Ethyl-3-methylpentanal

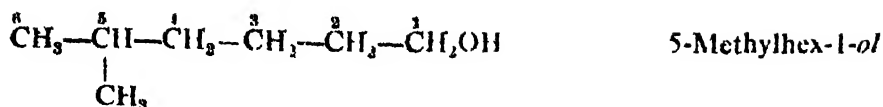
2.1.2a *Alcohols*: In naming alcohols the suffix *-ane* is changed to *-ol*, i.e., an *alkan-ol*. The numbering commences from that end of the chain which gives the lowest number to the $-\text{OH}$ group.



2-Chloro-1-ethanol



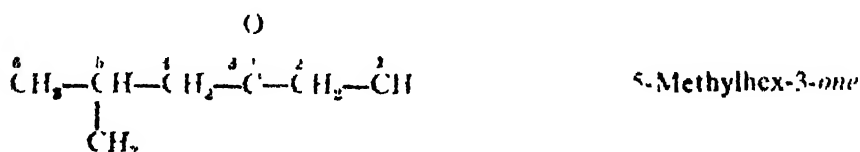
2-Propanol



2.2.2b Aldehydes: The suffix *-ane* is changed to *-al*, i.e., an alkanal. Since the carbonyl group occupies the terminal position, it is always the number 1 carbon atom.



2.1.2c Ketones: The suffix *-ane* is changed to *-one*, i.e., an alkanone. The numbering commences from that end of the chain which gives the lowest number to the carbonyl group. It is always necessary to prefix the name by a number to specify the position of the carbonyl group.



Naming of compounds containing other functional groups has been discussed in respective chapters.

2.1.3 Naming Compounds Containing Two Functional Groups

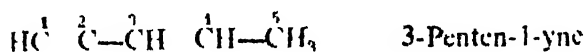
In a compound containing two functional groups, a general question is to decide the principal functional group. For this purpose there is no IUPAC rule. However, the system developed by chemical abstracts is followed. The fundamental rule is to use the principal functional group as *suffix* and indicate other substituents by *prefixes*. The selection of the principal functional group is made on the basis of the preference listed below:

1. Acids
2. Acid derivatives
(esters, halides, amides)
3. Aldehydes
4. Nitriles
5. Ketones
6. Alcohols
7. Thiols
8. Amines
9. Ethers
10. Acetylenes
11. Alkenes

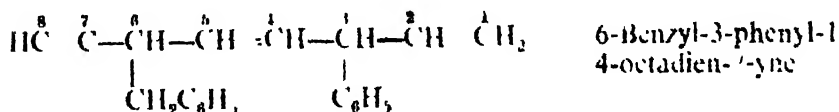
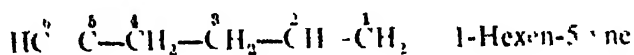
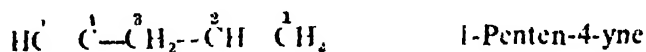
It must be remembered that when a double or triple bond constitutes one of the two functional groups, it can be used only as a *suffix*. In the following pages various examples will be discussed by taking different combinations of functional groups.

2.1.3a C=C and C≡C

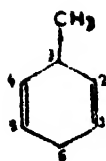
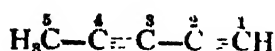
Two suffixes are used for a compound containing both the unsaturations and the compound is named an *alkenyne* with numbering as low as possible given to multiple bonds, the triple bond getting the lowest number.



If there is a choice then the double bond gets the preference over the triple bond in the numbering but the compound is still named an *alkenyne*. The double bond controls the numbering which is an exception to the general rule that the final suffix controls the numbering.



If two identical unsaturations or functional groups are present, then the compound is generally named in the same manner as a monofunctional compound. The typical group suffix is combined with the syllable *di-* to indicate the presence of two groups.

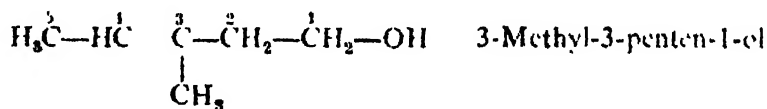
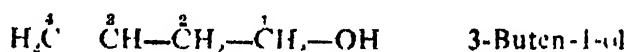
3-Methylcyclohexa-1
4-diene

1, 3-Pentadiyne

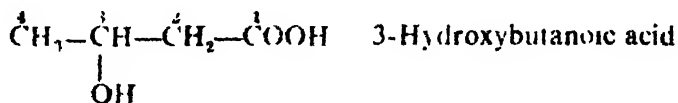
Note that if the *suffix* starts with a consonant (as in the above two examples) then the letter *a* is also attached.

2.1.3b C—C and —OH

The hydrocarbon *suffix* *-ene* and that of alcohol *-ol* are used as suffixes. The *-ol* gets the preference and the compound is named an *enol*

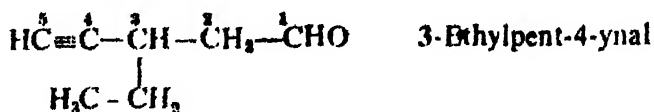


The —OH group is also used as a *prefix*.



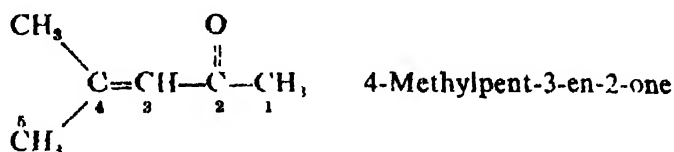
2.1.3c C=C and CHO, C≡C and CHO

The compounds are named an *alkenal* and an *alkynal* respectively. The —CHO group, being the principal functional group, governs the numbering.

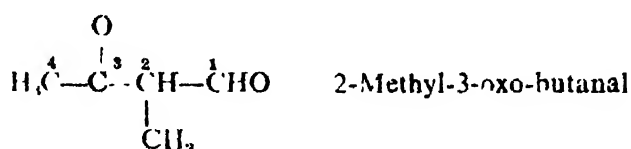


2.1.3d C=C and C=O; C≡C and C≡O

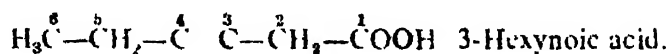
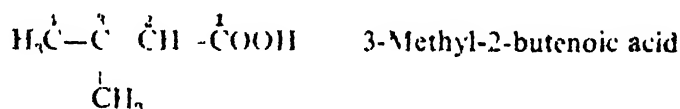
The compounds are named an alkenone and an alkynone respectively. The position of the keto group is indicated by a number along the carbon chain.



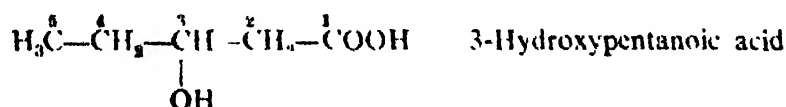
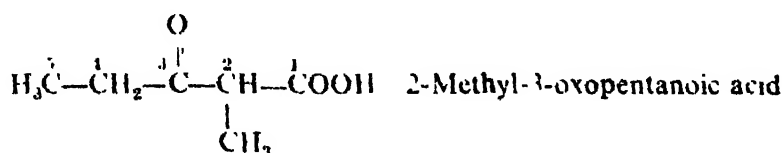
The C=O group is sometimes used as a substituent (oxo) alone with a number to indicate its position.

**2.1.3e C=C and COOH; C≡C and COOH**

The compounds are named an alkenoic and an alkynoic acid respectively.

**2.1.3f C=O and COOH; OH and COOH**

The carboxyl group takes precedence as the principal function group. The OH (hydroxyl) and C=O (oxo) groups are used as substituents, along with the number to indicate their positions.

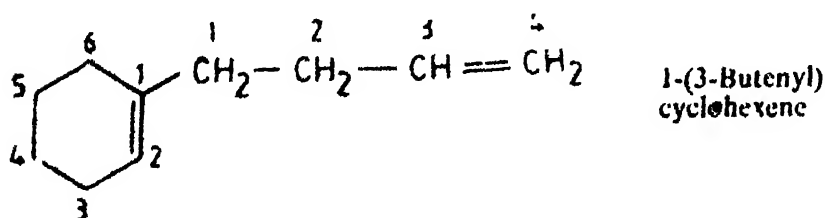
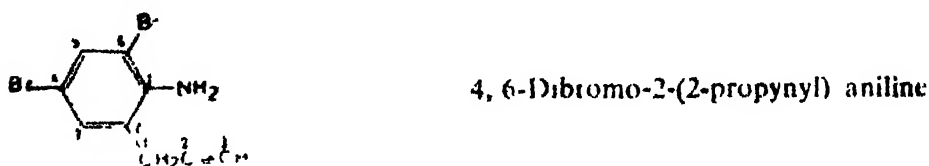
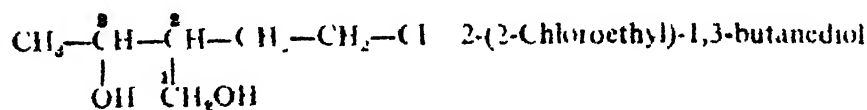
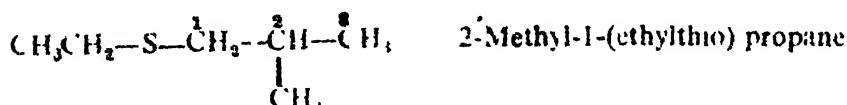
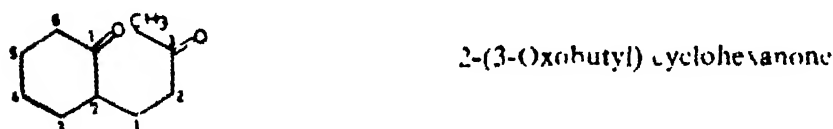
**2.1.3g OH and CN; C=O and CN**

The cyano group takes preference and its carbon atom is numbered 1.



2.1.4 Compounds Containing Two Chains

Certain compounds consist of two chains, i.e. a substituent attached to the main chain contains a numerical prefix. In such cases the name of the substituent is constructed using IUPAC nomenclature and this is enclosed within parentheses to separate the numbering of the substituent and the main carbon chain. The following typical examples will illustrate this point.



2.2 HOMOLOGOUS SERIES

In a series of a family of compounds containing the same functional group, all the members display similar chemical properties. Each member differs from the other by a methylene ($-\text{CH}_2$) group and is described by a general formula, such a series is called a *homologous series* (from the Greek, *homos*, the same and *logos*, proportion) and the individual member is referred to as *homologue*. Examples of homologous series with their trivial and IUPAC names are given in Table 2.3.

Table 2.3 Homologous Series

Formula	Trivial Name	IUPAC Name
1 Alkenes or Paraffin Hydrocarbons, General Formula C_nH_{2n}		
CH_4	Methane	IUPAC names same as the trivial names
CH_3CH_3	Ethane	
$\text{CH}_3\text{CH}_2\text{CH}_3$	Propane	
$\text{CH}_3(\text{CH}_2)_2\text{CH}_3$	Butane	
$\text{CH}_3(\text{CH}_2)_3\text{CH}_3$	Pentane	
$\text{CH}_3(\text{CH}_2)_4\text{CH}_3$	Hexane	
$\text{CH}_3(\text{CH}_2)_5\text{CH}_3$	Heptane	
$\text{CH}_3(\text{CH}_2)_6\text{CH}_3$	Octane	
$\text{CH}_3(\text{CH}_2)_7\text{CH}_3$	Nonane	
$\text{CH}_3(\text{CH}_2)_8\text{CH}_3$	Decane	
$\text{CH}_3(\text{CH}_2)_9\text{CH}_3$	Undecane	
$\text{CH}_3(\text{CH}_2)_{10}\text{CH}_3$	Dodecane	
$\text{CH}_3(\text{CH}_2)_{11}\text{CH}_3$	Tridecane	
$\text{CH}_3(\text{CH}_2)_{12}\text{CH}_3$	Tetradecane	
$\text{CH}_3(\text{CH}_2)_{13}\text{CH}_3$	Pentadecane	
$\text{CH}_3(\text{CH}_2)_{16}\text{CH}_3$	Eicosane	
$\text{CH}_3(\text{CH}_2)_{24}\text{CH}_3$	Triacontane	
$\text{CH}_3(\text{CH}_2)_{31}\text{CH}_3$	Tetracontane	
2. Alkenes or Olefins, General Formula C_nH_{2n}		
$\text{H}_2\text{C}=\text{CH}_2$	Ethylene	Ethene
$\text{H}_2\text{C}=\text{CHCH}_3$	Propylene	Propene
$\text{H}_2\text{C}=\text{CHCH}_2\text{CH}_3$	<i>n</i> -Butylene	1-Butene
$\text{H}_2\text{C}=\text{CH}(\text{CH}_2)_2\text{CH}_3$	<i>n</i> -Pentylene	1-Pentene
$\text{H}_2\text{C}=\text{CH}(\text{CH}_2)_3\text{CH}_3$	<i>n</i> -Hexylene	1-Hexene
3. Alkynes or Acetylenes, General Formula $\text{C}_n\text{H}_{2n-2}$		
$\text{HC}\equiv\text{CH}$	Acetylene	Ethyne
$\text{HC}\equiv\text{CCH}_3$	Methylacetylene	Propyne
$\text{H}_3\text{CC}\equiv\text{CCCH}_3$	Dimethylacetylene	2-Butyne

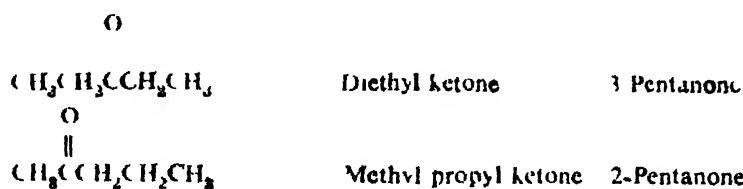
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Formula	Trivial Name	IUPAC Name
4. Alkyl Halides, General Formula $C_nH_{2n+1}X$ or RX, where $X = Cl, Br, I, F$		
CH_3Cl	Methyl Chloride	Chloromethane
CH_3CH_2Cl	Ethyl Chloride	Chloroethane
$CH_3(CH_2)_2Cl$	Propyl Chloride	Chloropropane
$CH_3(CH_2)_3Cl$	Butyl Chloride	Chlorobutane
$CH_3(CH_2)_4Cl$	Pentyl Chloride	Chloropentane
5. Alcohols, General Formula $C_nH_{2n+1}OH$ or ROH		
CH_3OH	Methyl alcohol	Methanol
CH_3CH_2OH	Ethyl alcohol	Ethanol
$CH_3(CH_2)_2OH$	Propyl alcohol	Propanol
$CH_3(CH_2)_3OH$	Butyl alcohol	Butanol
$CH_3(CH_2)_4OH$	Pentyl alcohol	Pentanol
6. Ethers, General Formula $ROR(R')$		
CH_3OCH_3	Dimethyl ether	Methoxymethane
$CH_3OCH_2CH_3$	Ethyl methyl ether	Methoxyethane
$C_2H_5CH_2OCH_2CH_3$	Diethyl ether	Ethoxyethane
7. Thiols (mercaptans), General Formula $C_nH_{2n+1}SH$ or RSH		
CH_3SH	Methanethiol	Methyl mercaptan
CH_3CH_2SH	Ethanethiol	Ethyl mercaptan
$CH_3(CH_2)_2SH$	Propanethiol	Propyl mercaptan
$CH_3(CH_2)_3SH$	Butanethiol	Butyl mercaptan
8. Aldehydes, General Formula $C_nH_{2n+1}CHO$ or $RCHO$		
$HCHO$	Formaldehyde	Methanal
CH_3CHO	Acetaldehyde	Ethanal
CH_3CH_2CHO	Propionaldehyde	Propanal
$CH_3(CH_2)_2CHO$	Butyraldehyde	Butanal
$CH_3(CH_2)_3CHO$	Valeraldehyde	Pentanal
$CH_3(CH_2)_4CHO$	Caproaldehyde	Hexanal
$CH_3(CH_2)_5CHO$	Heptaldehyde	Heptanal

9. Ketones, General Formula		
	$ \begin{array}{c} R \\ \diagdown \\ C \\ \diagup \\ (R') R \end{array} O $	
$ \begin{array}{c} O \\ \\ CH_3CCH_3 \end{array} $	Acetone	Propanone
$ \begin{array}{c} O \\ \\ CH_3CCH_2CH_3 \end{array} $	Methyl ethyl ketone	2-Butanone

(Contd.)

Formula	Trivial Name	IUPAC Name
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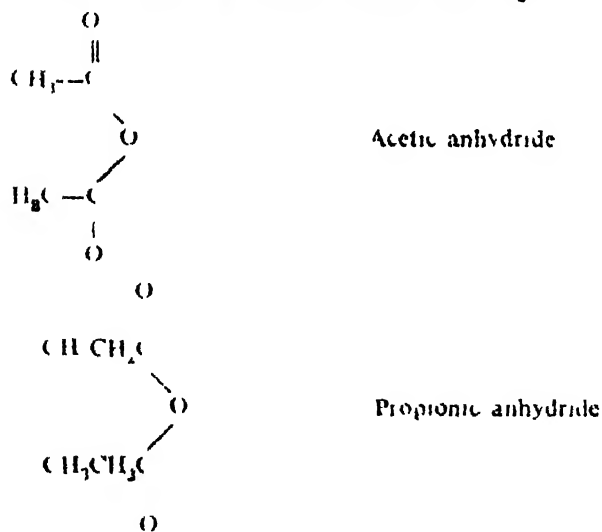


10 Carboxylic Acids, General Formula $\text{C}_n\text{H}_{2n+1}\text{COOH}$ or RCOOH

HCOOH	Formic acid	Methanoic acid
CH_3COOH	Acetic acid	Ethanoic acid
$\text{CH}_3\text{CH}_2\text{COOH}$	Propionic acid	Propanoic acid
$\text{CH}_3(\text{CH}_2)_2\text{COOH}$	Butyric acid	Butanoic acid
$\text{CH}_3(\text{CH}_2)_3\text{COOH}$	Valeric acid	Pentanoic acid
$\text{CH}_3(\text{CH}_2)_4\text{COOH}$	Caproic acid	Hexanoic acid

O

11 Acid Anhydrides, General Formula $(\text{RCO})_2\text{O}$








12. Acid Chlorides, General Formula RCOCl

$\begin{array}{c} \text{O} \\ \\ \text{HCCl} \end{array}$	Formyl chloride	Methanoyl chloride
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(Contd.)

Formula	Trivial Name	IUPAC Name
$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{CCl} \end{array}$	Acetyl Chloride	Ethanoyl Chloride
$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{CH}_2\text{CCl} \end{array}$	Propionyl Chloride	Propanoyl Chloride
$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{CH}_2\text{CH}_2\text{CCl} \end{array}$	Butyryl Chloride	Butanoyl Chloride
O		
13. Amides, General Formula RCNH_2		
$\begin{array}{c} \text{O} \\ \\ \text{HCNH}_2 \end{array}$	Formamide	Methanamide
$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{CNH}_2 \end{array}$	Acetamide	Ethanamide
$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{CH}_2\text{CNH}_2 \end{array}$	Propionamide	Propanamide
$\begin{array}{c} \text{O} \\ \\ \text{CH}_3(\text{CH}_2)_2\text{CNH}_2 \end{array}$	Butyramide	Butanamide
O		
14. Esters, General Formula RCOR (R')		
$\begin{array}{c} \text{O} \\ \\ \text{HCOCH}_3 \end{array}$	Methyl formate	Methyl methanoate
$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{COCH}_3 \end{array}$	Methyl acetate	Methyl ethanoate
$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{CH}_2\text{COCH}_3 \end{array}$	Methyl propionate	Methyl propanoate
$\begin{array}{c} \text{O} \\ \\ \text{CH}_3(\text{CH}_2)_2\text{COCH}_3 \end{array}$	Methyl butyrate	Methyl butanoate
$\begin{array}{c} \text{O} \\ \\ \text{CH}_3(\text{CH}_2)_3\text{COCH}_3 \end{array}$	Methyl valerate	Methyl pentanoate

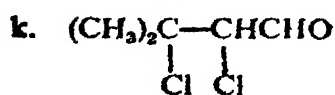
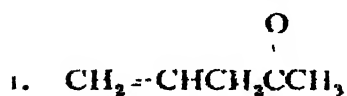
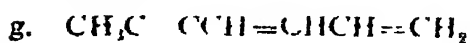
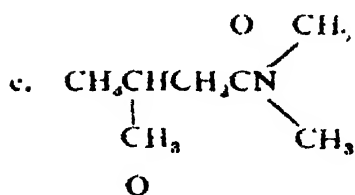
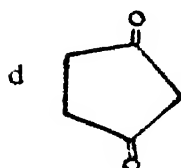
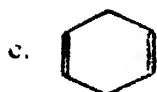
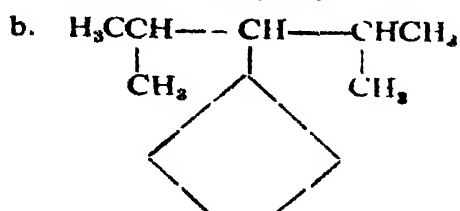
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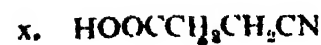
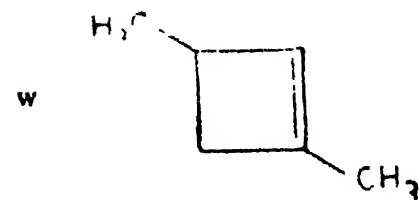
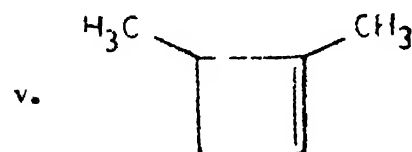
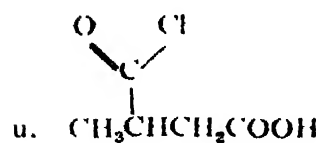
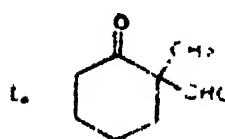
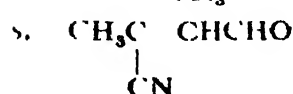
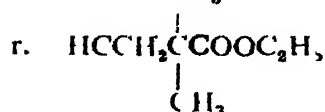
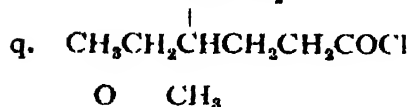
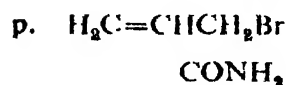
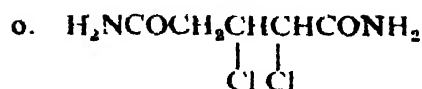
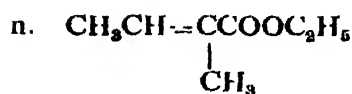
Formula	Trivial Name	IUPAC Name
15. Amines, General Formula $C_nH_{2n+1}NH_2$ or RNH_2		
CH_3NH_2	Methylamine	
$CH_3CH_2NH_2$	Ethylamine	
$CH_3(CH_2)_2NH_2$	Propylamine	
$CH_3(CH_2)_3NH_2$	Butylamine	
16. Alkyl Cyanides or Nitriles, General Formula $C_nH_{2n+1}CN$ or RCN		
HCN	Hydrogen cyanide	Formonitrile
CH_3CN	Methyl cyanide	Acetonitrile
CH_3CH_2CN	Ethyl cyanide	Propionitrile
17. Nitroalkanes, General Formula $C_nH_{2n+1}NO_2$ or RNO_2		
CH_3NO_2	Nitromethane	
$CH_3CH_2NO_2$	Nitroethane	
$CH_3CH_2CH_2NO_2$	Nitropropane	
$CH_3(CH_2)_3NO_2$	Nitrobutane	
$CH_3(CH_2)_4NO_2$	Nitropentane	
18. Alicyclic Hydrocarbons, General Formula C_nH_{2n}		
C_3H_6		Cyclopropane
C_4H_8		Cyclobutane
C_5H_{10}		Cyclopentane
C_6H_{12}		Cyclohexane
C_7H_{14}		Cycloheptane

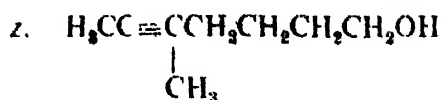
In the above Table the expression C_nH_{2n+1} has also been represented by the symbol R. It is obvious that a homologous series is characterized by a general molecular formula, difference of CH_2 between successive homologues and similarity in chemical behavior.

QUESTIONS

2.1 Write IUPAC names for the following structures







- 2.2 Write the structures as well as the correct names for the following compounds :
- 3-Pentyn-1-ene
 - 2-Allylbutanal
 - 3-Chloro-1, 3-butadiene
 - 5-Ethyl-3-methylheptane
 - 3-Butene
 - 3, 3-Dimethyl-1-propyne
 - 1, 3-Pentyne
 - Vinylacetic acid
 - 3-Oxo-7-octanol
 - Hex-2-en-6-ol
 - 3-Buten-1-yne
 - 2-Methyl propyl ethanoate
- 2.3 Define a functional group. Name some such groups containing an oxygen atom.
- 2.4 State the rules for IUPAC system of nomenclature of organic compounds with suitable examples.
- 2.5 Write structural formula for the following compounds :
- 3, 4, 4-Trimethylheptane
 - 3, 5-Octadiene
 - 2-Methyl-2-penten-1-ol

3

Factors Affecting Acid Base Strengths

The properties of a molecule are affected by its structure. This could happen either by the introduction of certain substituents or by the nature of the carbon chain linked to the functional group. These effects are often described in terms of resonance, inductive, steric and related electron shifts and the results are correlated with the experimental observations. After a brief review of acids and bases, various factors will be discussed which influence the acid base strengths of organic molecules.

3.1 ACIDS AND BASES

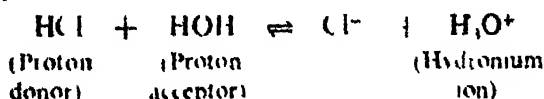
Many organic compounds behave as acids and bases. Several theories have been advanced to describe them.

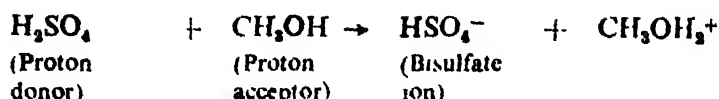
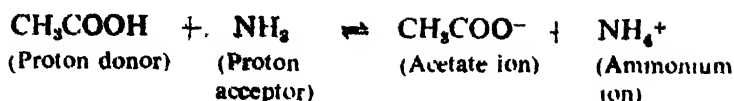
3.1.1 The Arrhenius Concept

An acid was defined as a substance which provides hydrogen ions on dissociation. Likewise, substances that yield hydroxyl ions by dissociation are classified as bases. One equivalent of an acid neutralizes one that of a base and the process is called *neutralization*. This definition, however, is limited in its scope because compounds like ammonia, pyridine, aniline, etc., also behave as bases though they are unable to yield hydroxyl ions.

3.1.2 The Bronsted-Lowry Concept

These workers independently defined an acid as a substance that can donate a proton and a base as that which can accept a proton. The strength of an acid is thus its tendency to donate a proton and the strength of a base is its tendency to accept a proton or the availability of an unshared pair of electrons for donation. This led to the concept of a conjugate acid-base pair. For instance, hydrogen chloride is the conjugate acid for the base (Cl^-) which in turn is the conjugate base for the acid hydrogen chloride. Water and the hydronium ion (H_3O^+) i.e. protonated water molecule have a similar relationship as the latter can also serve as a proton donor and is, therefore, a Bronsted acid. *

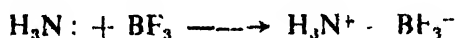




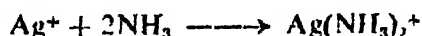
Accordingly, the stronger an acid, the weaker is its conjugate base; the stronger the base, the weaker is its conjugate acid. It thus follows that the equilibrium in any neutralization reaction would lie on the side of the weaker acid and base. A mineral acid is classified as a strong acid because its conjugate base has a low tendency to hold onto a proton.

3.1.3 The Lewis Concept

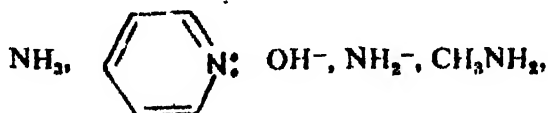
Lewis observed that certain compounds, though did not possess a hydrogen atom, still had acidic properties. He, therefore, proposed an extended view of acids. Accordingly an acid may be defined as any substance that is capable of accepting an electron pair. A base, on the other hand, is a substance that can donate an electron pair. Compounds like AlCl_3 , FeCl_3 , SnCl_4 , SO_3 , BF_3 , POCl_3 , Ag^+ , etc. function as Lewis acids. A neutralization reaction in Lewis terminology will be described as follows :



In boron trifluoride, the boron atom has already used its three L-shell electrons to form a covalent bond (sp^3 hybridized). Since this shell has four orbitals, a remaining fourth orbital is unoccupied in boron. This orbital thus accepts a pair of electrons from ammonia and can thus enter into bond formation. In addition, species that usually are not considered as acids, such as silver ions, are acids according to the Lewis definition because they can accept electrons. Silver ions, thus, can accept electrons when they react with ammonia.



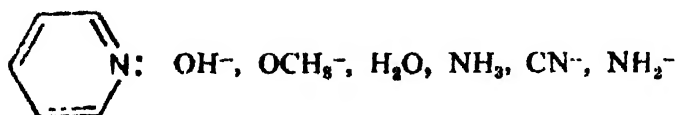
Though the definition of an acid differs in the Brönsted-Lowry and Lewis concepts, the description of a base is similar. Thus



etc. are bases according to both the concepts.

A reagent that is electron-deficient is termed an *electrophile* (or electron seeking) e.g. BF_3 , SO_3 , NO_2^+ , Cl^+ , Br^+ , etc., are electrophiles. A *nucleophile*

(nucleus seeking) is any reagent that has excess electrons, for example,



etc. are nucleophiles. In general, any anion is a nucleophile in varying degrees of nucleophilic strength

3.2 IONIZATION CONSTANT

The strength of an acid is determined in terms of its ionization *constant* or dissociation constant, K_a and for the dissociation of an acid HA , it is expressed by equation (3.1). The species are enclosed in square brackets to denote their molar concentrations.



Note that K_a is a unitless quantity. The value of K_a refers to the extent of proton donation. The larger the numerical value of K_a , the stronger the acid.

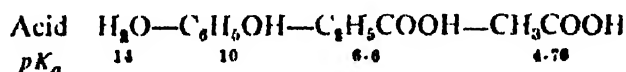
Since the ionization constant of different acids vary by many powers of ten, it is easy to handle them in a more convenient way, i.e. by using the negative logarithm of the dissociation constant, as expressed below:

$$pK_a = -\log K_a$$

The pK_a of an acid is, in effect, the pH of an aqueous solution in which the acid is half-ionized. The pK_a of acetic acid is 4.76 which is a more convenient expression than the ionization constant, 1.75×10^{-5} . The pK_b for a base can similarly be determined, and can then be converted into pK_a , if necessary by using equation (3.2).

$$pK_a + pK_b = 14 \quad (3.2)$$

The stronger an acid, the lesser is its pK_a value and the stronger a base, the greater is its pK_b . The following values demonstrate this point:



In this series as the strength of the acid increases, the pK_a progressively decreases. The concentration of hydrogen ions is expressed in terms of pH , as defined by equation (3.3).

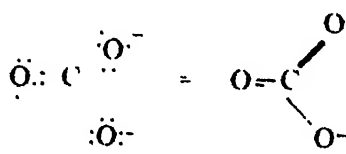
$$\text{pH} = -\log [\text{H}^+] = \log \frac{1}{[\text{H}^+]} \quad (3.3)$$

The magnitude of pH is a measure of the acidity of dilute aqueous solutions of acids but cannot be used to characterize the acidity of concentrated acids accurately. The Hammett acidity function H_0 has been proposed as an extension of the pH scale for concentrated acids. Its discussion is beyond the scope of this work.

In the following pages we will discuss the various factors that are responsible for the acidity and basicity of organic compounds

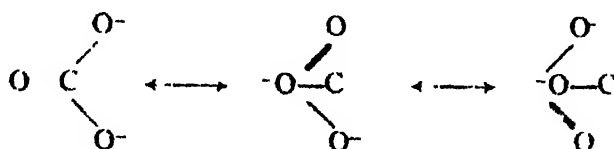
3.3 RESONANCE

In many cases it is not possible to describe the electronic structure of a species adequately with a single Lewis structure. Consider, for example, the carbonate ion (CO_3^{2-}). The Lewis structure, in which the position of



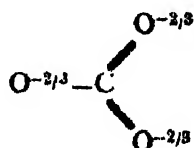
Electronic structure Lewis structure

the electrons is fixed, shows that there are two C—O single bonds and one C=O double bond. It has experimentally been determined that the three carbon—oxygen bond lengths in carbonate ion are equal and the bond distance is equal to 1.28 Å. Two more structures, in fact can be written for the carbonate ion as shown below.



Such structures which differ in the arrangement of electrons only are called resonance structures and this phenomenon is known as *resonance*. A *resonance hybrid* is a true structure composed of all the possible contributing structures. Resonance is always a stabilizing factor.

The carbonate ion has the following hybrid structure :



A resonance hybrid is more stable, i.e. it has a lower internal energy than any of its contributing structures. The resonance structures are represented by means of a double headed arrow (\longleftrightarrow) and each structure is said to contribute to the resonance hybrid. A resonance structure is written by shifting the positions of electrons; in reality no such movement of electrons takes place, the different structures are only arbitrary.

Delocalisation or the shift of electrons in a molecule always decreases the energy and enhances its stability. The *resonance energy* is thus a measure of the stability of a system, and it is described as the difference between the actual energy of the resonance hybrid and the energy of the most stable contributing structure. The resonance energy is determined indirectly by taking an appropriate model compound that is available and which, we have reason to believe, approximates the required compound. A most appropriate model for benzene is cyclohexene and the frequently used method for the determination of resonance energy is hydrogenation of this compound. Thus, if cyclohexene is reduced catalytically, the heat of hydrogenation is 28.6 Kcal/mole.



Similarly for benzene the heat of hydrogenation equals 49.6 Kcal/mole. It



may now be argued that benzene should evolve three times the amount of heat of hydrogenation compared to cyclohexene, i.e. 3×28.6 or 85.8 Kcal/mole. But the experimentally determined value is 49.8 Kcal/mole. Therefore, the difference of 36 Kcal/mole is attributable to the extra stability in the benzene molecule due to resonance. This can be schematically be described on a diagram (Fig. 3.1).

Table 3.1 Resonance Energy (Kcal/mole) of some Organic Molecules

Benzene	36
Naphthalene	16
Anthracene	83.5
Cyclooctatetraene	4.8
Fulvene	11.0
1, 3-Butadiene	3.5

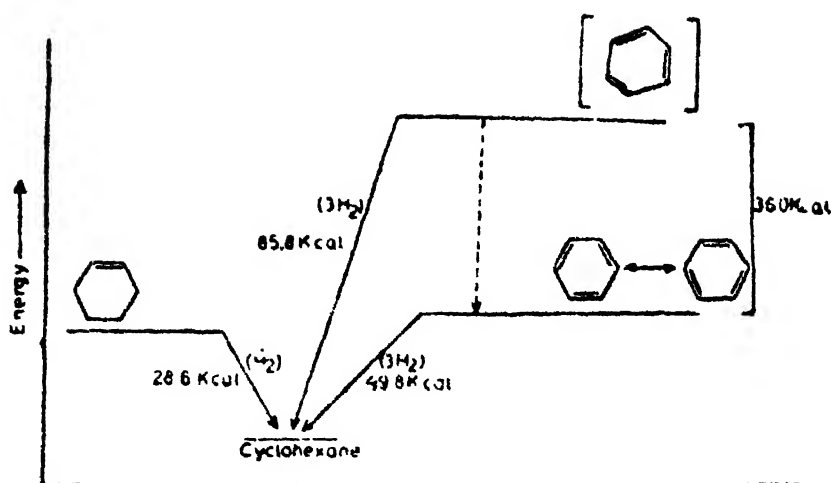


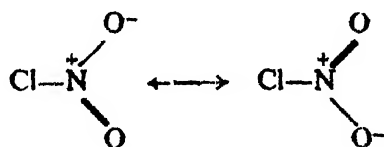
Fig. 3.1 Estimation of the Resonance Energy of Benzene Molecule

Resonance energies for some simple molecules are recorded in Table 3.1.

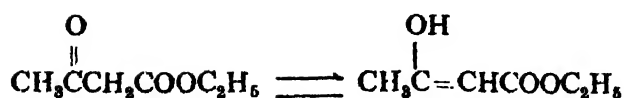
The following rules may be noted while attempting to write resonance structures for a compound.

1. For resonance structures to be written the molecule should be planar and possess an alternating system of single and double bonds, such as in benzene and naphthalene. Cyclooctatetraene, on the other hand, is non-planar and possesses a low resonance energy.

2. The relative positions of atomic nuclei in the contributing structures should remain unchanged. Nitryl chloride (NO_2Cl) has the following two resonance structures:

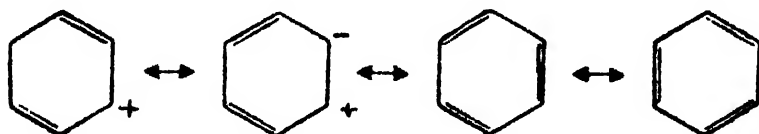


but the following two structures for acetoacetic ester are no longer resonance structures because the position of the hydrogen atom has been changed.



They instead represent two different molecules and the relationship between the *keto* and *enol* forms is known as *keto-enol tautomerism*.

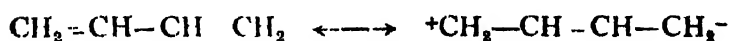
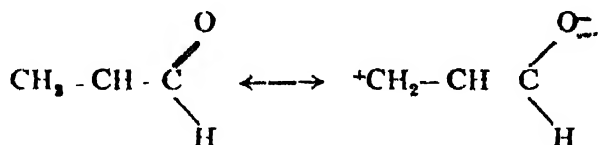
3. Only structures of the lowest energies contribute significantly to resonance.



This applies to structures that involve charge separation, as charged structures, having higher energies, contribute insignificantly to the resonance hybrid. For benzene, the last two charged structures make little contribution to resonance.

4. The resonating part of the molecule should be planar, i.e. all atoms should lie in a plane for the purpose of writing its resonance structures.

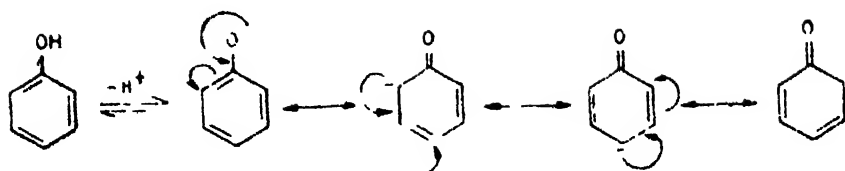
5. Resonance structures that carry a negative charge comparatively on a more electronegative atom are more stable than those in which the charge is located on a less electronegative atom. Thus, between propenal and 1, 3-butadiene, the latter has a lower resonance energy because the negative



charge is located on the carbon atom compared to oxygen in propenal.

The effect of resonance or delocalization of electrons in a molecule on the acidity and basicity of molecules will be evident from the following examples.

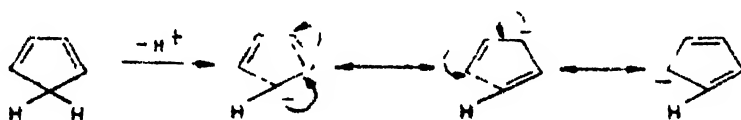
Both phenol and ethanol contain $-\text{OH}$ group and thus would be expected to be acidic. Indeed both are acidic, phenol reacts with strong bases (NaOH) while alcohol forms salts with electropositive metals (Na) only. But phenol ($K_a=10^{-10}$) is much more acidic than alcohol ($K_a=10^{-16}$). This difference in acidity is explained by considering the fact the phenoxide ion is stabilized by resonance, while ethoxide ($-\text{OC}_2\text{H}_5$) is not. The different resonance structures for phenoxide ion may be written as follows:



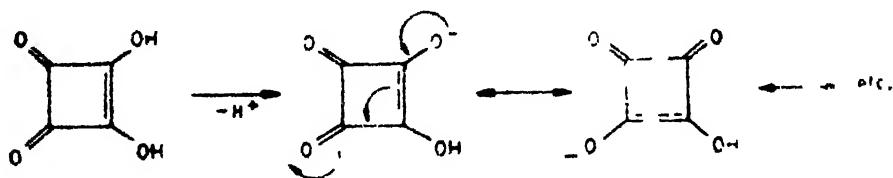
The acidic nature of phenol is reflected by its common name *carbolic acid*. Thus it may be concluded that if the ion is stabilized by resonance than the parent compound is acidic. Although phenol is more acidic than alcohol it is less so than carboxylic acids ($K_a \sim 10^{-8}$); This is the reason why phenol does not react with sodium carbonate or sodium bicarbonate. The acid strengths of phenols can be enhanced by the presence of electron-withdrawing substituents such as NO_2 at the *ortho*- and *para*-positions of the ring. An electron-withdrawing group assists in dispersing the negative charge of the phenoxide ion by resonance and thus stabilizes the anion.

Picric acid (2, 4, 6-trinitrophenol) is comparable in strength ($K_a = 1$) to inorganic acids. Electron-donating groups, on the other hand, tend to decrease acidity.

Cyclopentadiene contains an acidic hydrogen as the cyclopentadienyl anion is stabilized by resonance.

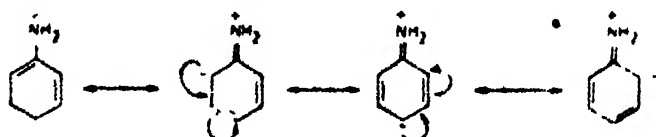


An interesting example of an acidic compound is squaric acid which is highly acidic ($K_a = 10^{-1}$) and is comparable in strength to sulfuric acid.

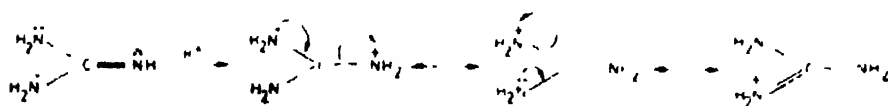


Resonance stabilization of the ion explains its high acidity.

The basicity of organic molecules is similarly influenced by resonance. Aniline ($K_b = 5.4 \times 10^{-10}$) is less basic than ammonia ($K_b = 2 \times 10^{-5}$) because the electron pair on the nitrogen atom in aniline is less available for donation due to resonance with the ring.

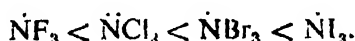


In Lewis terminology the capacity of electron donation determines the basicity of a molecule. Alternatively it may be argued that the basicity of aniline is low because the anilium ion or the conjugate acid is not stabilized by resonance. On the other hand, guanidine is highly basic because the protonated amine is stabilized by resonance.



Guanidine is among the strongest organic bases known. In general, aromatic amines are much less weaker than aliphatic amines and ammonia.

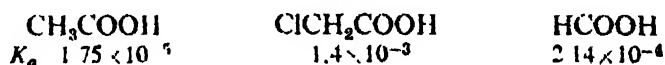
For the same reason the basicity of the following amines increases in the order :



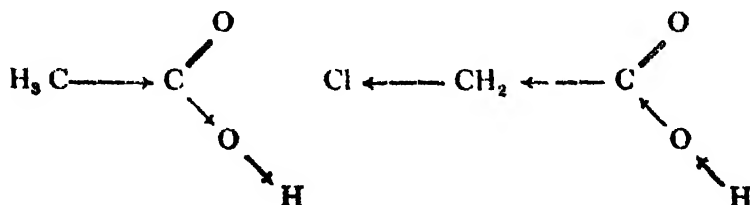
Iodine is the least and fluorine is the most electronegative in the halogen series

3.4 INDUCTIVE EFFECT

Besides conjugation or resonance, there is an additional way for the transmission of electrons. This is done in the classical sense *via* the *inductive effect* in which the electrical effects are propagated in a chain by successive polarization of carbon-carbon σ -bonds. This happens when electron donating or withdrawing groups are attached to the chain. The concept can be easily understood by an example. Consider, acetic and chloroacetic acids of which the latter is a stronger acid. The higher acidity of chloroacetic acid is attributable to inductive effect. The chlorine atom on chloroacetic acid



relative to hydrogen atom in acetic acid assists in loosening the O—H bond



by pulling electrons towards itself due to its high electronegativity as shown above. The electrons are shifted closer to the oxygen atom in chloroacetic acids, thus weakening the O—H bond and making the proton easily remova-

ble. The chlorine atom has thus affected the acidity of chloroacetic acid by creating an electron deficiency at the carboxyl carbon atom. Between acetic and formic acids, the former is still weaker because the methyl group in acetic acid is a better electron-releasing group than hydrogen in formic acid. Inductively an electron-withdrawing group, thus, has an acid strengthening effect and an electron-donating group, an acid weakening effect.

The larger the electron-withdrawing inductive effect, the greater is the acidity. As a result fluoroacetic acid is stronger than bromoacetic acid, because fluorine is considerably more electronegative than bromine.



$$K_a = 21 \times 10^{-3}$$



$$K_a = 2.85 \times 10^{-3}$$

Moreover, the inductive effect is additive and among the chloroacetic acids, trichloroacetic acid is the strongest because of the presence of three chloro-groups.



$$K_a = 2.24 \times 10^{-1}$$



$$5.02 \times 10^{-2}$$



$$1.4 \times 10^{-3}$$

Since this effect is transmitted along a chain, the effect falls off with distance, as is evident from the ionization constants of the following acids. The acid in which the chlorine atom is closer to the carboxyl group is stronger because it can pull the electrons more effectively.



$$K_a = 1.5 \times 10^{-3}$$

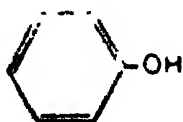


$$8.12 \times 10^{-5}$$

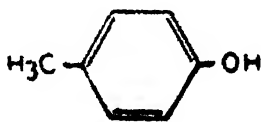


$$3.02 \times 10^{-5}$$

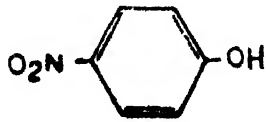
The acidity of phenols and aromatic carboxylic acids is also modified by inductive effects, the electron-donating groups decreasing and the electron-withdrawing groups increasing the acidity. This effect thus operates in a similar manner to resonance in aromatic compounds.



$$K_a = 1.02 \times 10^{-10}$$



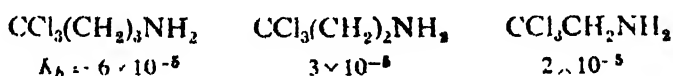
$$6.45 \times 10^{-11}$$



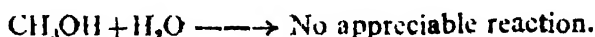
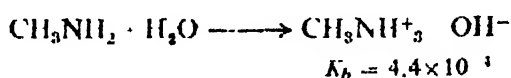
$$6.50 \times 10^{-8}$$

The inductive effect works in an opposite direction for bases in comparison to acids i.e. electron-donating groups increase while electron-withdrawing groups decrease basicity. Methylamine, for example, is more basic than ammonia because of the electron donating methyl group which increases the electron density on the nitrogen atom. On the basis of inductive effect

alone, the basicity of amines may be interpreted as $\text{Me}_3\text{N} > \text{Me}_2\text{NH} > \text{MeNH}_2 > \text{NH}_3$, because trimethylamine has three electron-donating methyl groups and the others have correspondingly less number of methyl groups. This order is, however, incorrect because besides the structural effects, the solvent, by solvation of an ion may also influence acidity or basicity. Solvation by the solvent surrounding an ion has an important stabilization effect. A solvent, depending on its polarity can orient around the ion to form *clusters* and thus stabilize it. But if large groups are present on the amine, they can cause reduced solvation and resultant destabilization of the ion. The large groups prevent the approach of the solvent to the ion because of *steric effects*. Such effects also have noticeable influence on the ionization constants of both acids and bases. The basicity order of the above amines thus decreases in the order: $\text{Me}_2\text{NH} > \text{MeNH}_2 > \text{Me}_3\text{N} > \text{NH}_3$, i.e. Me_3N is a weaker base than either Me_2NH or MeNH_2 due to steric effects. In trimethylamine, the three methyl groups cause hindrance to the solvation of the ion. Electron-withdrawing groups, on the other hand, tend to decrease the basicity; this is obvious from the following series of amines. In *monochloromethylamines* the $-\text{CCl}_3$ group is situated nearer to the amino group and withdraws electrons more efficiently thus decreases its

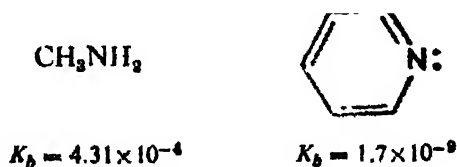


basicity. Base strength also decreases with increasing electronegativity of the atom bearing extra electron pair. This is due to the fact that elements of higher electronegativity attract the unshared electron pair closely to themselves making them less available for bonding. For this reason methyl alcohol is a weaker base than methylamine



3.5 HYBRIDIZATION EFFECTS

Hybridization effects alter basicity as they effect electronegativity and bond lengths. An oxygen or nitrogen atom having multiple bonding is rendered less basic. This may be explained by comparing the basicity of methylamine and pyridine. In the aliphatic amine, the non-bonding pair of electrons is in an sp^3 orbital while in a compound containing a double bonded nitrogen,



it is an sp^3 orbital. The electrons in an s orbital are more firmly bonded than in a p orbital because the former are closer to the nucleus. Since the amount of s character increases with unsaturation, the electrons in pyridine (sp^3 hybridized) are more tightly bound and are not easily available for bonding.

Thus pyridine is less basic than methylamine. Guanidine $\left(\begin{array}{c} \text{H}_2\text{N} \\ \text{H}_2\text{N} \end{array} \right) \text{C} \text{NH}$ in contrast, is a strong base because of resonance of the protonated base.

QUESTIONS

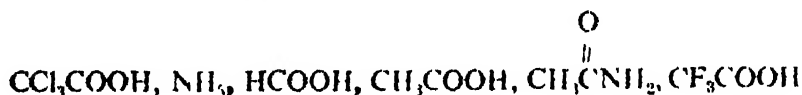
- 3.1 (a) Would $\text{BrCHCH}_2\text{COOH}$ be a stronger acid than



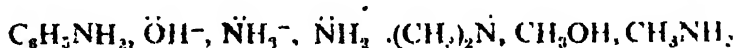
$\text{BrCH}_2\text{CH}_2\text{COOH}$? Why ?

- (b) Why is the compound $(\text{CF}_3)_3\ddot{\text{N}}$ virtually non-basic ?

- 3.2 (a) Write the following in the increasing order of acid strength



- (b) Write the following in the decreasing order of base strength

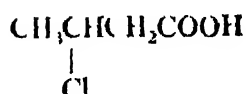
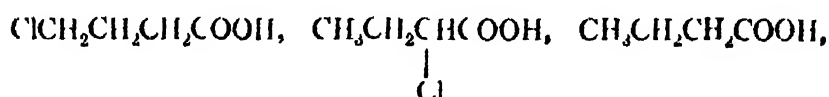


Give reasons for your answer in both cases

- 3.3 Write short notes on the following:
Solvation, resonance energy, electrophiles, nucleophiles, Lewis acids, tautomerism and resonance hybrid.
- 3.4 2, 4, 6-Trinitrotoluene is a relatively acidic compound. Explain why the proton is easily removed from the methyl group ?
- 3.5 (a) State the Lewis concept of acids and bases.
(b) Can a proton (H^+) be regarded as an acid according to Bronsted and Lewis definitions ?
- 3.6 (a) The heat of hydrogenation of 1-butene is 30.3 Kcal/mole and that of 1, 3-butadiene is 57.1 Kcal/mole. Calculate the resonance energy of 1, 3-butadiene.
(b) Can 2-butene be chosen as a model instead of 1-butene in the above case ?
- 3.7 Classify the following into Lewis acids, bases or neither:



- 3.8 What do you understand by electrophilic and nucleophilic reagents? Give examples of each
- 3.9 Arrange the following in decreasing order of acidity phenol, *p*-cresol and *p*-nitrophenol. Give reasons for your answer.
- 3.10 Explain the important principles of the concept of resonance. Discuss the application of resonance to (a) structure of benzene, (b) stability of phenylmethyl radical, and (c) color of triphenylmethane dyes
- 3.11 Trifluoroethanol is 1000 times more acidic than ethanol. Explain.
- 3.12 Neither pure H_2SO_4 nor HClO_4 conduct an electric current. Explain.
- 3.13 (a) Which is a stronger acid and why?



- (b) Which is a stronger base and why?



- 3.14 Write resonance structures for the following molecules



- 3.15 Write an expression for the acidity constant (K_a) of benzoic acid and show that pK_a is equal to the pH of a half-ionized aqueous solution

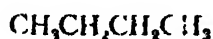
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Stereoisomerism

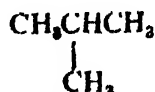
The chemical investigation of organic molecules requires a knowledge of the strength of bonds. An additional important aspect of such a study is the detailed structure of molecules and *stereochemistry* concerns itself with their three dimensional geometry. An understanding of stereochemistry is one of the most powerful tools that a chemist can make use of to determine the course of a chemical reaction. The most stable covalent bonds are formed with a preferred three dimensional orientation. A *structural formula* for a compound conveys which atom is directly linked to which other atom. It, however, tells nothing about the shape of the molecule but indicates the groups of elements present which provide clues to the properties of the substance.

4.1 ISOMERISM

Different compounds with the same molecular formula but different physical and chemical properties are called *isomers* and the general phenomenon is known as *isomerism*. There are two types of isomerism, namely, structural isomerism and stereoisomerism. Compounds which possess the same molecular formula but differ in structure are *structural isomers* and the phenomenon is termed as *structural isomerism*. This is further sub-divided into three types, namely *chain isomerism*, in this type the isomers differ in the variation of the carbon chain or skeleton of the molecule, for instance, butane and isobutane. They differ in the structure of their carbon chains. *n*-Butane is unbranched while *iso*-butane is branched.



n-Butane



iso-Butane

If the molecules have the same molecular formula but differ in the type of the functional group present then it is known as *functional group isomerism*. Functional group isomers belong to different homologous series. A few examples of this type of isomerism are the following :

$\text{C}_2\text{H}_5\text{OH}$
Ethyl alcohol

and

CH_3OCH_3
Dimethyl ether

$\text{CH}_3\text{CH}_2\text{COOH}$
Propionic acid

and

O
 CH_3COCH_3
Methyl acetate

In *positional isomerism*, the isomers differ in the attachment of the functional group to the chain in different positions. This is illustrated by the following examples.

$\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$

and

CH_3CHCH_3
|
OH

Propyl alcohol

iso-propyl alcohol

$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl}$ and

$\text{CH}_3\text{CH}_2\text{CHCH}_3$
|
Cl

Butyl chloride

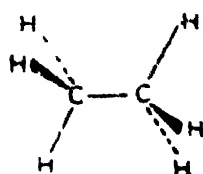
sec-Butyl chloride

The second type of isomerism called *stereoisomerism* is concerned with the arrangement of atoms of a molecule in space. They are not structural isomers. This is classified into two types, i.e. optical and geometric isomerism. In these types, the molecules have the same molecular formula but differ in the spatial arrangement of groups, i.e. they differ in configuration. This will be discussed later in the chapter.

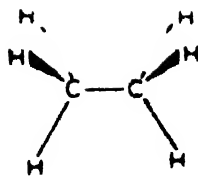
4.2 CONFORMATION AND FREE ROTATION

In a majority of molecules, the individual groups or atoms can take up different positions with respect to one another because of free rotation about the carbon-carbon single bond. Molecules which differ from each other only as a result of rotation about the C—C bond are called *conformers*. *Conformation* implies the actual three dimensional arrangement of the groups on one carbon with respect to those at the other carbon atom in the molecule. Obviously, an infinitely large number of such conformers can exist, corresponding to different degrees of rotation about the C—C bond. *Conformational analysis* is a study of the energy changes that occur in a molecule when groups rotate about single bonds. Generally, only three types are considered. Certain conformations of a molecule are energetically more stable than the other. The first type, fully *staggered* conformation in which the bulky groups are as far apart as possible is the most stable.

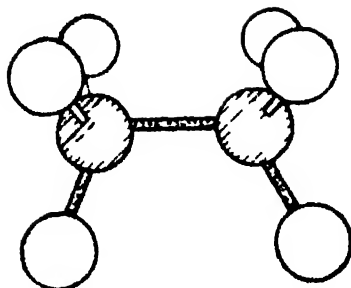
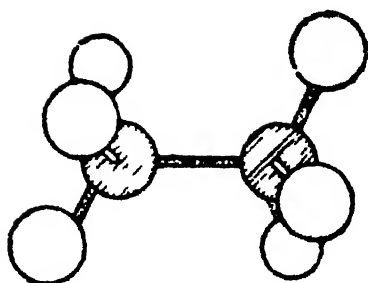
The *staggered* and *eclipsed* (second type) in which the groups are close together conformations of ethane are shown as *sawhorse* structures and below them are the ball and stick models of the same conformers.



Staggered



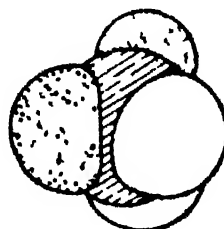
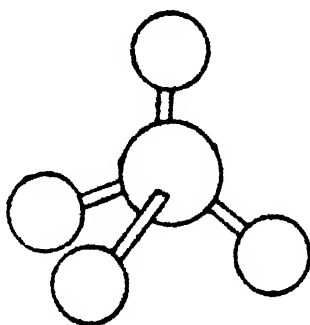
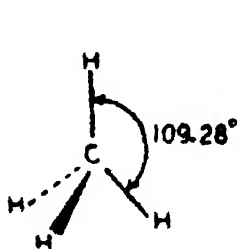
Eclipsed



Ball and Stick models of ethane

The third type is the *gauche* or *skew* conformation in which the bulky groups make a dihedral angle of 60° .

It was noted previously that in an sp^3 hybridized molecule the four bonds are directed at an angle of 109.28° . The three dimensional arrangement for methane, for instance, is shown in which the solid lines indicate that these



Methane (Dreiding model)

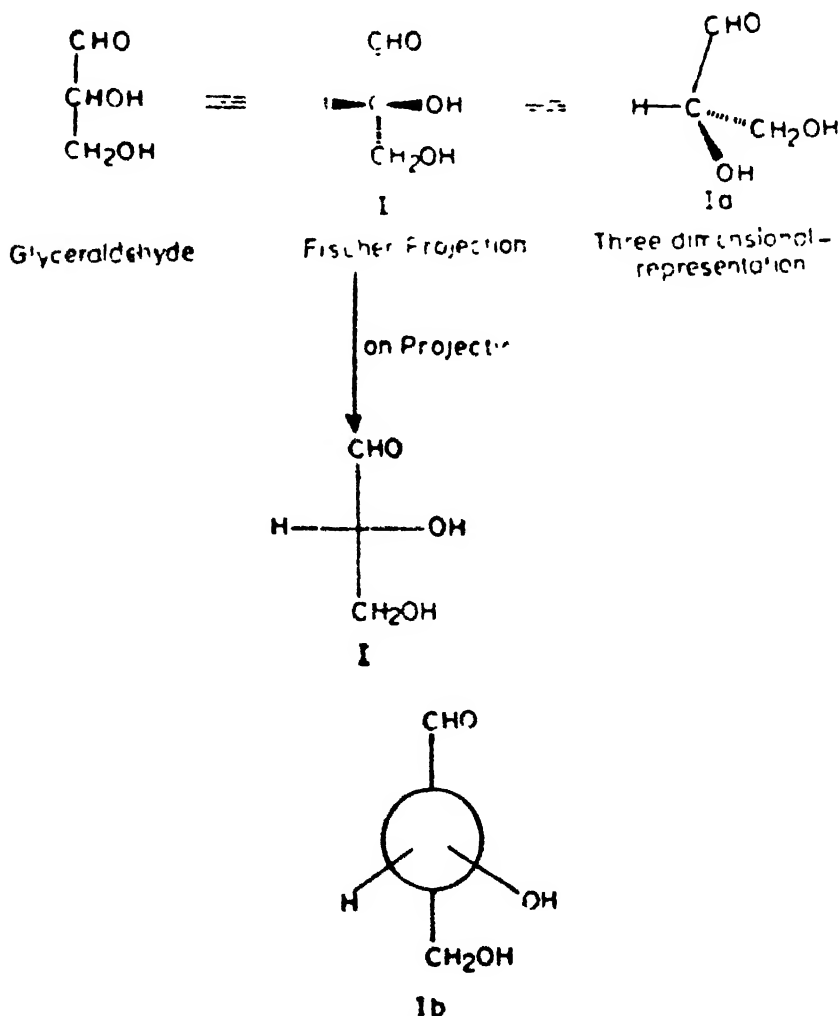
A ball and stick model

Stuart Briegleb model

bonds lie in the plane of the paper, the solid wedge means that this bond is projecting out of the plane of the paper towards the reader and the dashed line implies that this bond extends below the plane of the paper. These pictures are attempts to represent three dimensional molecules in a two dimensional plane. Two other types of models, namely the ball and stick and the Stuart-Briegleb models are also shown. Fischer in 1891, proposed a type of projection formula for representing tetrahedral carbon atoms on

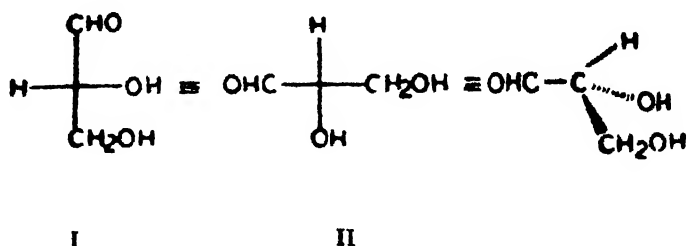
paper (i.e. as a two dimensional structure). According to this, the molecule is so oriented that the central carbon atom lies in the plane of the paper and the bonds on the right and left conventionally lie above while the other two (i.e. vertical bonds) below the plane. Also, the most important functional group is placed at the top and the main chain of the molecule is vertical. This can be demonstrated by taking glyceraldehyde as an example.

In another type of representation (Ib), the asymmetric carbon, i.e. the central carbon atom attached to four different atoms or groups, is considered as a sphere, the CHO and the CH₂OH groups lie towards the backside of the sphere. The remaining groups H and OH are projecting forward.

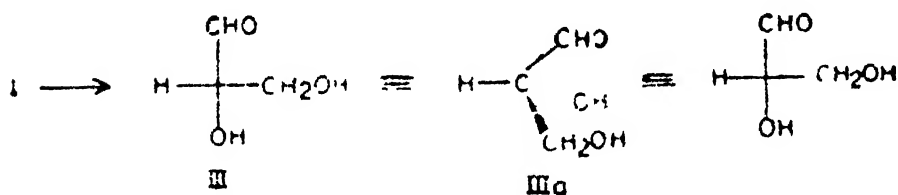


In the Fischer formulation, structure (I), the molecule is projected in the shape of a plus sign. *Fischer projection* is easy to write but the principal drawback is that one has to keep in mind that it is a planar projection of a

three-dimensional figure. In order to convert one *Fischer projection* to another identical structure, any two pairs of substituents need to be interchanged. But if instead only one pair of group is interchanged, a projection of its enantiomer (Sec. 4.3) is obtained. For glyceraldehyde, these conversions are formulated below :



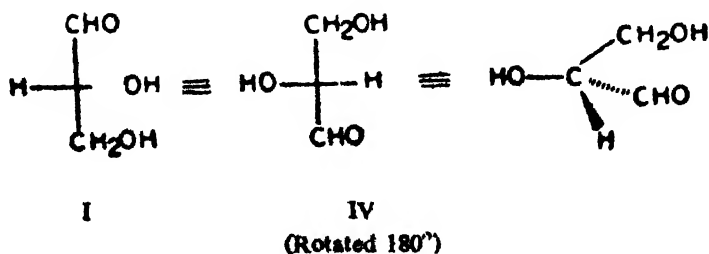
(Two Pairs of Groups Interchanged)

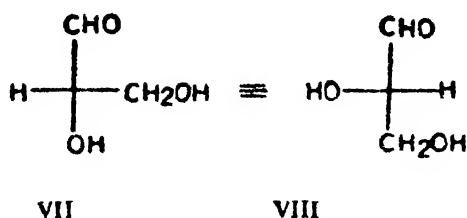
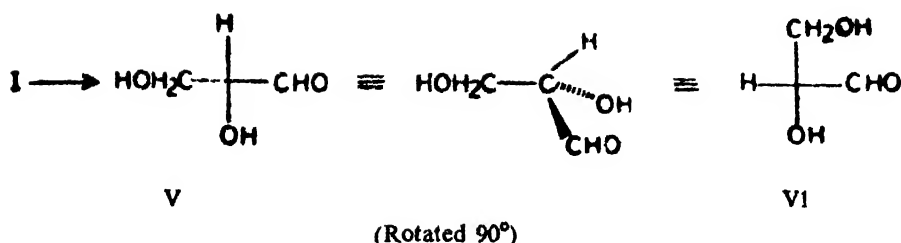


(One Pair of Groups Interchanged)

Structures (I) and (II) are identical while (I) and (III) are enantiomers of each other. Structures (III) and (IIIa) are similar.

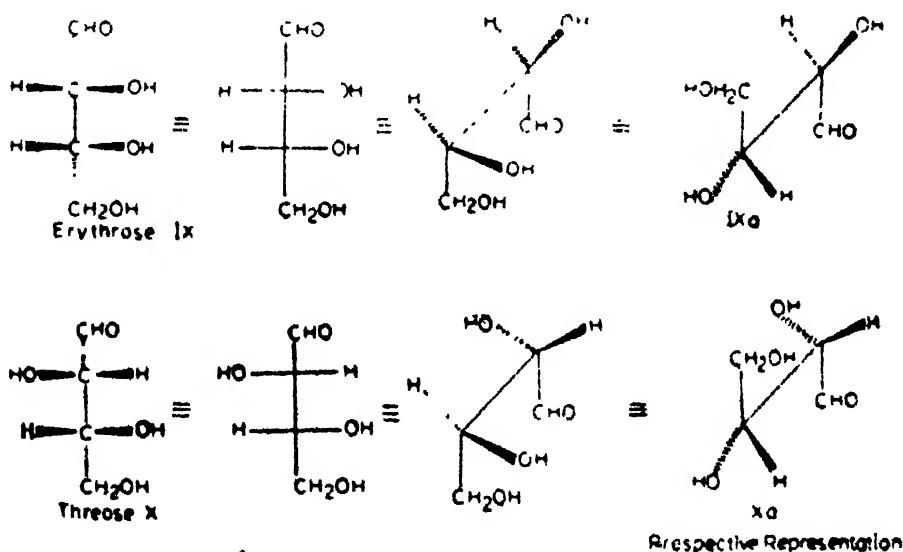
A *Fischer projection* formula may be rotated in the plane of the paper by 180° but not by 90° or 270° . Moreover, the formula should not be lifted out of the plane of the paper (i.e. it should be rotated around a pivot) to convert it into an identical structure. This is illustrated again taking glyceraldehyde as an example :





Structures (IV) and (V) are enantiomers and (V), (VI), (VII) and (VIII) are all the same.

For compounds containing two asymmetric atoms, the *Fischer projection* is obtained in the usual way. The asymmetric carbon atom lies in the projection plane and the horizontal groups project out and vertical substituents constituting the main chain of the molecule extend below the plane of the paper. It is customary to place the aldehyde group at the top and the carbinol group at the bottom as shown below in the case of *threose* and *erythrose*.

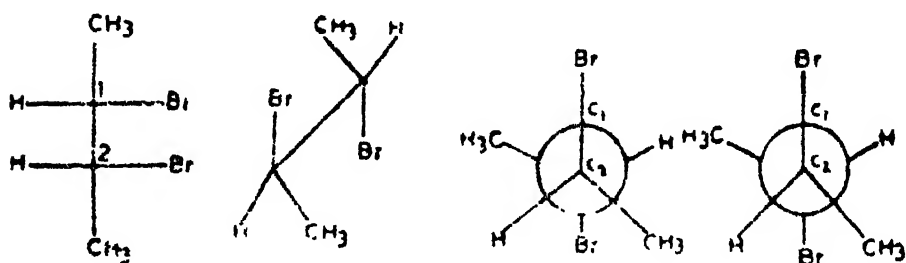


The nomenclature for molecules of such structures is derived from sugars, i.e. *erythrose* (IX) and *threose* (X) and are named by using the prefixes

erythro and *threo* depending upon whether the two sets of substituents of identical or like composition are situated on the same or opposite side, *respectively*. The *Fischer projection* for molecules of two asymmetric centres depicts the eclipsed conformation (view the molecule along the bonding line of the two carbon atoms). The substituents, however, tend to stay as far apart as possible; this is more clearly visualized by the *perspective representations* [skew forms, (IXa) and (Xa)]. These two structures represent a pair of enantiomers

A more useful and simple representation related to projection formula is the *Newman projection formula*.

In order to write the Newman projection formula, the two adjacent carbon atoms are marked C_1 and C_2 . The molecule is then viewed along the



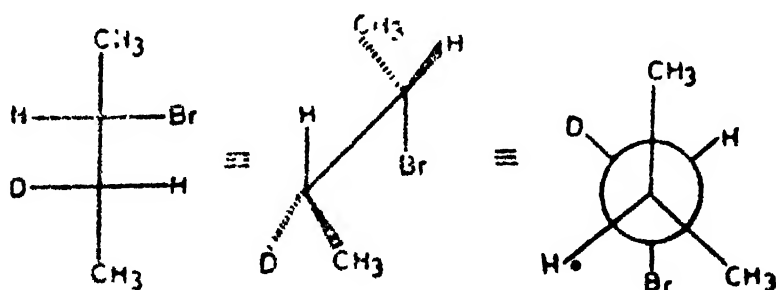
Fischer Projection

Perspective

Newman Projection

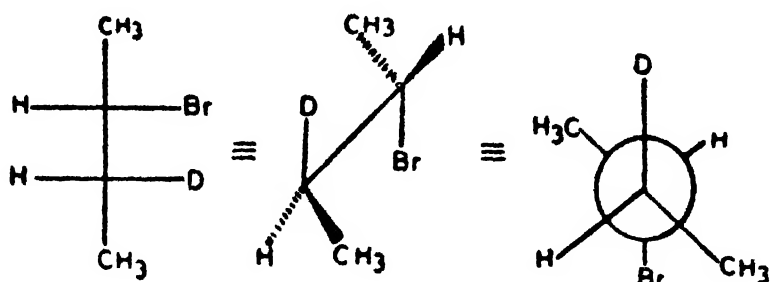
Staggered Form

C_2 - C_1 axis, as is shown for *meso*-2,3-dibromobutane. Carbon atom C_2 (nearer to the eye) is represented by a point and C_1 (away from the eye) by a circle and the bond between C_2 and C_1 is not seen. The three groups attached to C_2 radiate as three lines from the point and those at the periphery come from C_1 . The groups are then written in the same clockwise order on each carbon atom. Following these instructions, structure (XII) is obtained for dibromobutane. From this structure it is clear that a rotation of 60° about the C-C axis converts this staggered form to an eclipsed structure. The *Newman projection formula* is useful in representing the staggered conformation



Threo XIII

more vividly. Unlike the *Fischer projection* which is more difficult to visualize, the *Newman projection* can help decide more easily whether the conformation is *threo* or *erythro*. The translation process of one notation into another is summed up in the following example of 2-bromobutane-3-d.



Erythro XIV

Conformations are the result of free rotation about the carbon-carbon single bond. In ethane, the barrier to rotation about the C—C bond called the *torsional strain* is very small (2.8 Kcal/mole), therefore, at room temperature, the thermal energy is enough to make the rotation free. If one of the hydrogen atoms is replaced by another sizable group, the barrier increases. In monochloroethane, for instance, it amounts to 3.56 Kcal/mole, while in butane it rises to 5.5 Kcal/mole. In butane, the potential energy of the molecule varies with the angle of rotation with respect to the two methyl groups. The shape of potential energy curve with regard to the angle of rotation is drawn in Fig. 4.1. In order to discuss the conformational

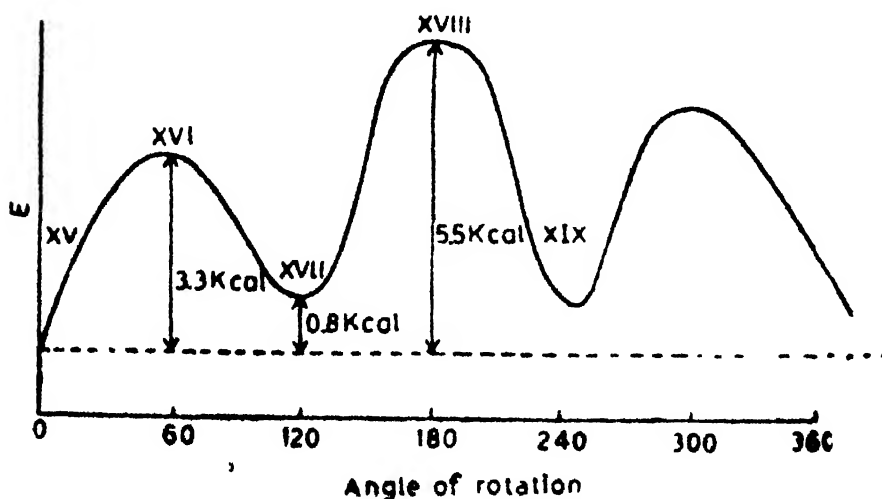
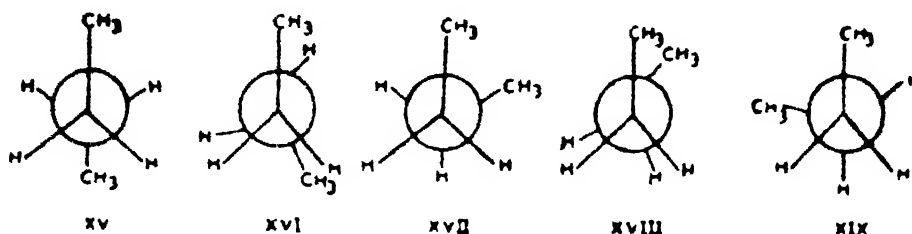


Fig. 4.1 Conformation Energy Barrier to Rotation about Carbon-Carbon Single Bond in Butane

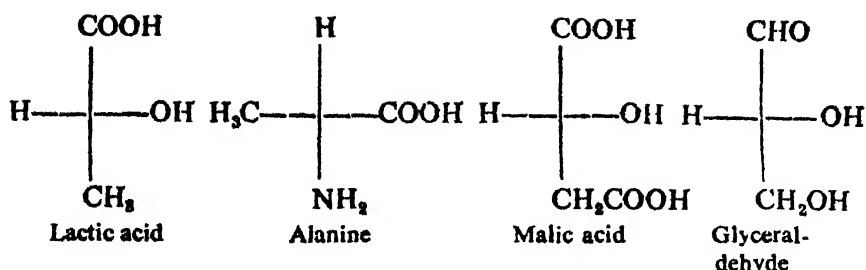
analysis of butane. Let us rotate the molecule from its most stable conformation when the like groups are as far apart as possible, i.e. the fully staggered form which is known as the *anti* or *trans* conformation (XV). This conformer will have the lowest energy. Rotate by 60° , and a conformation (XVI) is obtained in which there are two H—CH₃ and one H—H interactions and the barrier to rotation is small and is of the order of 3.5 Kcal/mole. This is an eclipsed conformation and comparatively less stable. Two more staggered conformations (XVII) and (XIX), are obtained, in



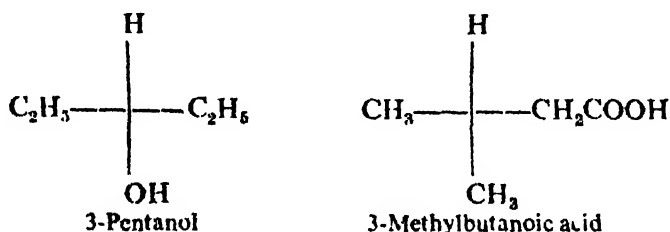
which the two methyl groups attached to carbons 2 and 3 make a dihedral angle of 60° . These are called *gauche* or *skew* forms and are 0.8 Kcal/mole higher in energy than the *anti* form (XV). At room temperature, butane is often a mixture of 72% *anti* and 28% *gauche* conformation. The second eclipsed conformation (XVIII) has one CH₃—CH₃ and two H—H eclipsed interactions. This is a fully eclipsed form and is 5.5 Kcal/mole less stable than (XV).

4.3 OPTICAL ISOMERISM

Pasteur, during his studies, noted that there were a number of organic compounds of similar structure which possessed the same physical and chemical properties but differed in the rotation of a beam of plane polarized light. Thus, there were two lactic acids which showed the same melting point (26°) but had an equal and opposite effect upon the plane polarized light. Such substances which are able to rotate the plane of polarized light, are said to be optically active. The basis for this type of isomerism was independently explained in 1874 by H. Van't Hoff (Nobel prize for Chemistry, 1901) of Netherlands and A. LeBel of France. They suggested that a regular tetrahedron with four different groups at each corner exists in two forms that are mirror images to one another. In other words, the optical activity was linked to the presence of an *asymmetric* carbon atom, i.e. one to which four different groups were attached. The term *chiral center* is preferred nowadays and compounds which are optically active are *chiral*. Chiral molecules must be asymmetric or dissymmetric. Subsequently, a large number of compounds were found to possess optical activity, some examples are as follows:

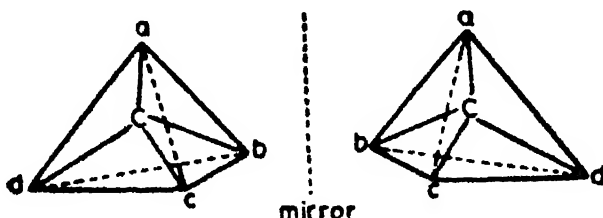


All these chiral compounds have two possible configurations, i.e. a particular arrangement of groups around the carbon atom in space and are mirror images of one another. On the other hand, the following compounds show no optical activity and are achiral.



It is also inferred that they have only one configuration. A molecule becomes symmetric if it contains two identical groups. A coffee cup, a cricket ball and a screw driver, etc. are some familiar objects which are symmetric.

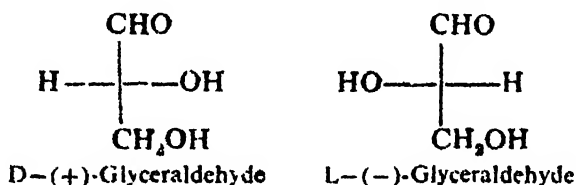
Pasteur, in 1847, further showed that optical isomerism in a molecule occurs in pairs. When four different atoms or groups are attached to the same carbon atom, two different structural arrangements are possible which are non-superimposable. Let us assume that the four groups are a, b, c and d, comprising the molecule Cabcd and the two resultant arrangements are the following:



If a mirror is placed between them it is found that one molecule is the mirror image of the other and the two are not superimposable. One isomer rotates the plane of polarized light in one direction and the second in the opposite direction. These two types of two different molecules are referred to as *enantiomers*. Enantiomers are also called optical isomers or optical antipodes. The enantiomeric structures differ in the configuration of groups at one asymmetric center only. The fact that enantiomers cannot be superimposed on one another raises a question—in exactly what way do they

differ structurally? The answer is that the two isomers differ only in the relative directions in which the four groups on the central carbon project into space. We say they have opposite configurations. Thus, the essential feature for a molecule to exhibit optical activity is *disymmetry*, i.e. a property of non-superimposability of an object on its mirror image. It will be observed that in bringing any two groups in coincidence in an enantiomeric pair, the remaining two groups will always fail to coincide. The human hand, a glove and a measuring cup, etc., are all disymmetric. To classify the corresponding optically active isomers, the one which rotates the plane of polarized light to the right is known *dextro* rotatory and is designated (+) or *d* and the one which rotates plane polarized light to the left is called *levo* and designated (-) or *l*.

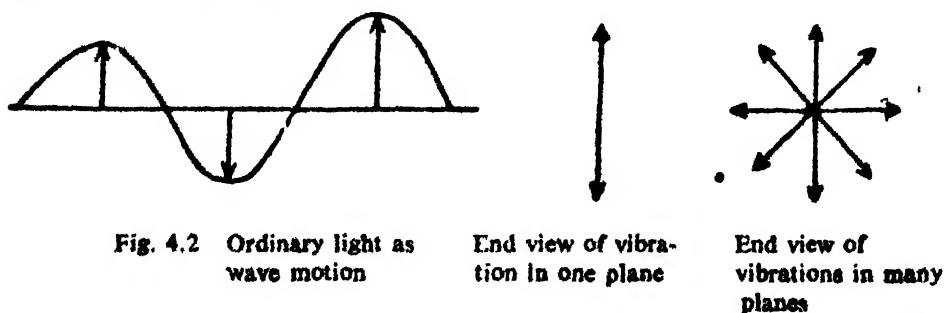
The two optically active forms of glyceraldehyde are represented below:



Both are known compounds. On the basis of these two compounds, scientists have developed the concept of configurational families. Any compound that has a configuration like that of (+)-glyceraldehyde and can be related to (+)-glyceraldehyde by known chemical reactions is said to belong to the D-family (that is, the hydroxyl group is written to the right of the asymmetric carbon). The mirror image of any compound in the D-family belongs to the L-family (that is, the hydroxyl group is on the left). The capital letters D and L are simply family names and have nothing to do with the actual signs of rotation. The optical isomers are distinguished by a polarimeter.

4.3.1 Plane Polarized Light

An ordinary beam of light (described as a wave motion) vibrates in all directions. A *plane polarized light* is one which vibrates entirely in one direction. An ordinary beam of light can be converted into a beam of plane polarized light by a device called a *polarizer*. The polarizer blocks all the components



of the beam except those waves that are polarized in one particular direction. The polarizer can be constructed from one of several materials such as *calcite* (a form of CaCO_3), a nicol prism or a polaroid. The extent of rotation due to optical activity is measured by a *polarimeter*. In its simplest form, it is a long cylindrical tube containing various parts. A beam of light (usually from a sodium lamp, $\lambda = 589 \text{ nm}$), passes through the polarizer (a nicol

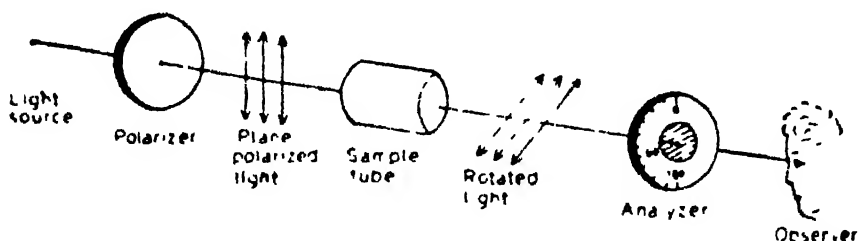


Fig. 4.3 Schematic representation of a polarimeter

prism) which emerges plane polarized. The light then passes through the solution of the sample contained in a tube. The light coming out still vibrates in one plane but the plane is tilted due to rotation of the plane of polarization, so that it lies at a different angle than it did originally. It is then allowed to pass through a second nicol prism called the *analyzer* having the same orientation as the first. This is done before the sample is placed in the instrument, the analyzer is lined up with the polarizer so that the polarized light vibrates in a vertical plane and can pass on through the analyzer. After the light passes through the sample it is no more aligned in a vertical plane and the light is blocked by the analyzer to a certain extent.

In order to allow the polarized light to pass freely, the analyzer must thus be rotated so that it is tilted at the same angle as the emerged polarized light from the sample. For this purpose the analyzer is mounted on a circular dial marked in degrees. The angle of rotation for maximum light to pass through the sample is recorded.

The extent to which a pure enantiomer will rotate the plane polarized light depends on several factors such as length of the sample tube (l , decimeters), sample concentration (c , mg/l), wave length (λ) of the light used, solvent and temperature. The measurement is reported in terms of *specific rotation* (α) expressed mathematically in equation (4.1).

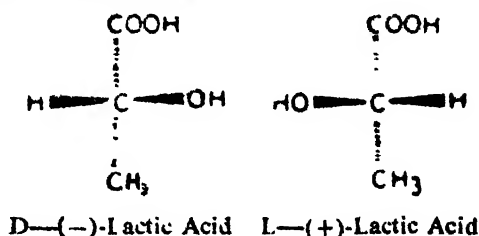
$$\left[\alpha \right]_{\lambda}^t = \frac{\theta}{l \times c} \quad (4.1)$$

where θ represents the observed rotation.

4.3.2 Lactic acid

Lactic acid is α -hydroxypropionic acid and occurs in sour milk and pickles. Commercially, it is obtained by the fermentation of sugar solution with the

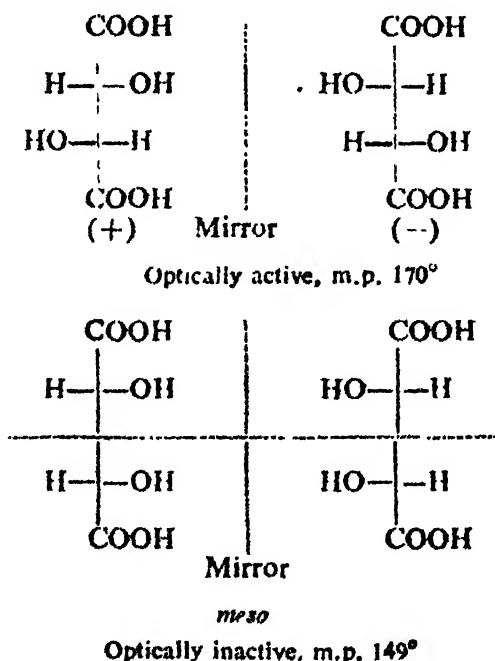
lactic acid *bacillus*. The synthetic or commercial acid is racemic and may be resolved into its enantiomers as explained in Sec. 4.4. The two isomers have the following configurations:



These configurations have been determined with reference to (+)-glyceraldehyde. When D-(---)-glyceraldehyde is converted to lactic acid by a sequence of reactions without breaking any bond linked to the asymmetric carbon atom, *levo* lactic acid is obtained.

4.3.3 Molecules with Two Asymmetric Atoms

In general the number of optically active isomers is given by the expression 2^n , where n implies the number of asymmetric centers. Thus 3, 4-dimethyl-4-phenyl-3-hexanol, $\text{CH}_3\text{CH}_2\text{C}(\text{CH}_3)(\text{C}_6\text{H}_5)\text{C}(\text{OH})(\text{CH}_3)\text{CH}_2\text{CH}_3$ exists in four enantiomeric forms. Molecules which contain two like asymmetric carbon atoms give fewer than $2^2 = 4$, optical isomers. A classical example is that of tartaric acid which has the following stereoisomers:



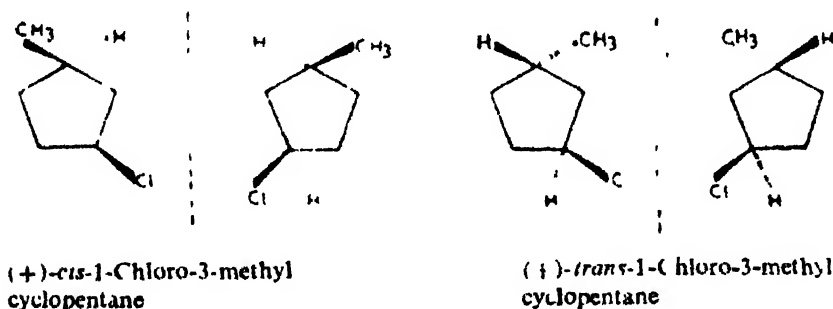
Each asymmetric atom has the same four groups, i.e. —H, —OH, —COOH and —CH(OH)COOH. The first two structures are non-superimposable and

are thus optically active and constitute an enantiomeric pair. The last two structures, however, have a plane of symmetry as shown, and as a result, the optical activity of the top half of the molecule is exactly cancelled by the other half. The compounds show a net rotation of zero and are identical and optically inactive. This form is called the *meso* form. The *meso* form is a diastereomer of each of the enantiomeric form.

The *meso* form is internally compensated and is thus optically inactive. It cannot be resolved into its optically active components. Though the formula 2ⁿ predicts four isomers for tartaric acid, only three are known. Two of them are an enantiomeric pair, m.p. 170°, and the third is the *meso* form, m.p. 140°. Similarly, 2, 3-dichlorobutane exists in three forms.

Diastereomers are defined as any pair of stereoisomers which are not enantiomers. Unlike enantiomers, diastereoisomers can differ in physical and chemical properties.

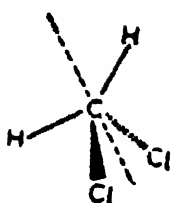
In contrast to an enantiomeric pair, the atoms and groups in a diastereomeric pair do not have the same relative spatial orientation. In the following structures, the *cis* enantiomers are diastereomeric with both the *trans*-enantiomers:



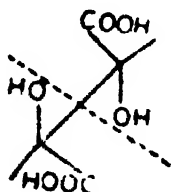
The rotation of one enantiomer is observed to be identical in magnitude but opposite in sign to the rotation of the other. If two optically active compounds are mixed in equal amounts, the rotation caused by one is cancelled exactly by the other so that the net optical rotation is zero. Such a mixture is known as a *racemic mixture* and is designated (\pm) or *dl*. A racemic mixture can be resolved into its enantiomers and the process is called *resolution*.

4.3.4 Symmetry Elements

The symmetry of a molecule arises because of the presence of certain symmetry elements. A molecule is said to possess a *plane of symmetry* if a plane drawn through the molecule bisects it into two halves such that one half is the mirror image of the other. This is shown for 1, 1-dichloromethane. A cup, fork, plate and a leaf all have at least one plane of symmetry. A *center of symmetry* in a molecule is said to exist if a line drawn from any group to this point and then extended an equal distance beyond this point,



it meets the mirror image of the original group. A compound with a center of symmetry usually has a *meso*-form, as shown for tartaric acid.



4.4 RESOLUTION

A racemic mixture (racemic modification) is obtained either from synthesis or a natural source. It can be separated into its optical isomers by any one of the following methods. *Resolution* is thus a separation of a mixture containing equal quantities of enantiomers into its components.

1 Mechanical Separation

Resolution can be effected by this method if the optical isomers have distinct crystals. The crystals then can be separated mechanically by a tweezer. Pasteur accomplished the resolution of tartaric acid in this manner. He allowed a dilute solution of the sodium ammonium salt of the acid to crystallize below 27° . Large crystals were thus obtained. Separation of the isomers was possible because the two types of crystals were hemihedric and had different orientations. This method has been useful in only a few cases.

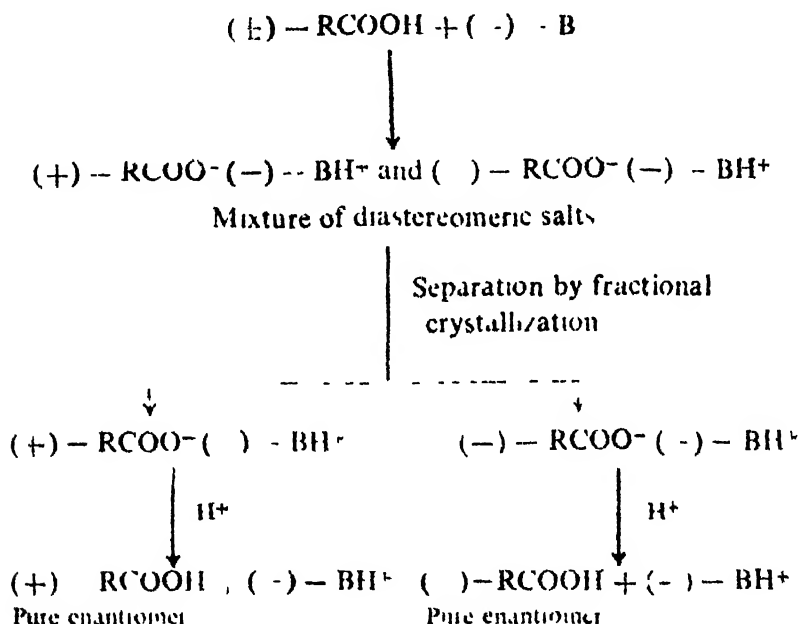


2. Formation of Diastereoisomeric Salts or Derivatives *

This is the most general method for the resolution of racemic mixture. The principle of this method involves the conversion of the mixture into its diastereoisomers by treatment with a previously resolved compound, often a

naturally occurring optically active reagent. Since diastereoisomers have different physical properties, they can be separated by physical means. A racemic mixture (\pm) A, for instance, is treated with a base ($--$) B with the resultant formation of two diastereoisomeric salts, $(+)-A:(-)-B$ and $(--)-A:(-)-B$. Since the diastereoisomers will have different physical and chemical properties, they can be separated by conventional methods and the enantiomers regenerated in a subsequent step.

This method is most suitable for the resolution of carboxylic acids or amines. Several naturally occurring optically pure alkaloids such as quinine, brucine, strychnine, etc. are available in a *levo* rotatory form. The following procedure can be adopted, assuming we have a racemic mixture of carboxylic acids, say lactic or tartaric acid:



Among the acids used for resolving amines are $(-)$ -malic acid, $(+)$ -tartaric acid, $(+)$ -camphoric acid, etc.

3. Enzymatic Resolution

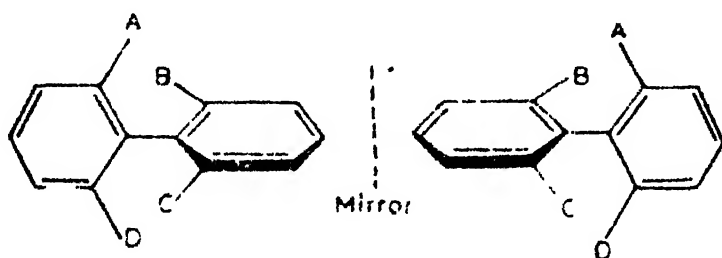
Enzymes are complex protein catalysts and are produced in the living organisms. A typical property of enzymes is their high stereoselectivity. They have been frequently used in biochemical synthesis to obtain highly pure compounds. Certain enzymes, if allowed to grow in the presence of a racemic mixture, often convert one of the isomers preferentially while the other remains untouched. Pasteur discovered that when a racemic mixture of ammonium tartrate was treated with *penicillium glaucum*, it resulted in the destruction of the $(-)$ -isomer only. The main limitation to this method is that since one of the enantiomers is destroyed, other techniques are still required to obtain it.

4. Kinetic Method

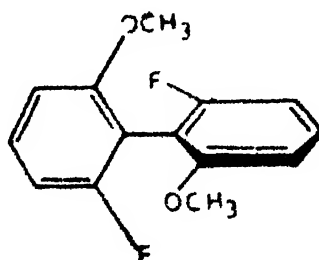
This method depends on the principle that the two diastereomers may be formed or react with a reagent at different rates because of the differences in free energy. An established example of this type is the partial resolution of (–)-mandelic acid with (–)-menthol. The *dextro* isomer reacts much faster than the *levo* isomer. When the reaction is interrupted before completion, (–)-menthyl (–)-mandelate predominates in the reaction mixture. The esterified acid yields predominantly (–)-mandelic acid, after hydrolysis.

4.5 OPTICAL ISOMERISM DUE TO RESTRICTED ROTATION

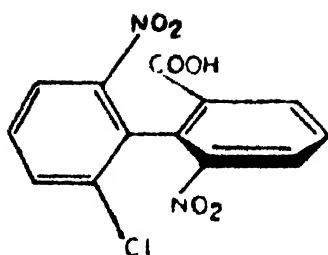
In examples considered earlier, optical activity was caused by the presence of an asymmetric center and non-superimposability of the mirror images. Certain molecules, however, are still optically active even if they do not contain a chiral center. An interesting class of such compounds includes that of biphenyl derivatives. Presence of bulky groups at the *ortho* positions of the molecule prevents free rotation around the carbon-carbon single bond joining the two rings because of steric interactions between the 2, 2' and 6, 6' pairs of groups. This type of steric crowding accounts for the molecular asymmetry and the resultant optical activity of these compounds. Polysubstituted diphenyl derivatives have been resolved into optical isomers, since the mirror images, as shown below, are not superimposable.



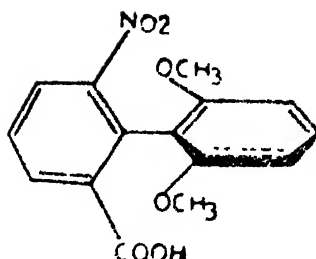
The two major conditions are that the substituents should be bulky and the rings be unsymmetrically substituted. Some examples are listed below:



Not resolved (free rotation)

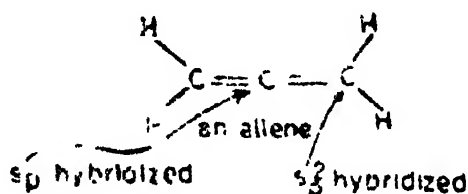


Resolved (unsymmetrical)

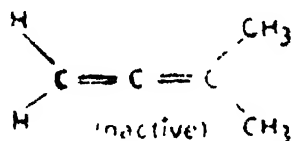


Not resolved (symmetrical)

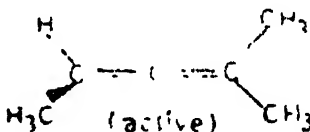
Another familiar class of compounds are *cumulenes* which contain adjacent double bonds. The simplest of these are known as *allenes*, and of these 1,2-propadiene may be represented as follows:



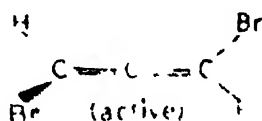
Allenes are rigid and can be resolved provided each terminal carbon atom is dissymmetric.



1,1 Dimethylallene

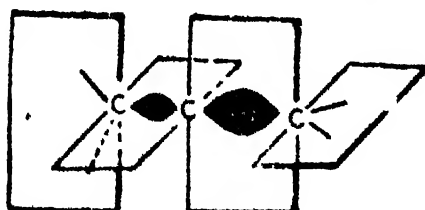


Penta-2,3-diene



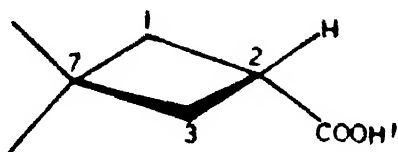
1,3 Dibromo propa 1,2-diene

The molecular dissymmetry is possible because the groups at one end of the molecule lie in the plane of the paper, while at the other end they lie perpendicular to it as depicted in the following diagram.



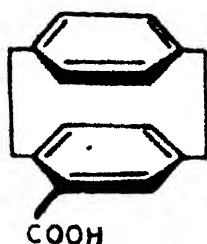
Therefore, the two sets of groups will be non-coplanar. If different groups are attached at each end, there will be no plane of symmetry. The compound will show optical activity. For the last two compounds, the mirror images are not superimposable and they are capable of existing as (+) and (−) enantiomers.

Another class of compounds that show optical isomerism are the *spiro* compounds, i.e. bicyclic ring systems in which the two rings have one carbon atom in common. A simple case of such a compound which has been resolved is given below. The plane of one ring lies perpendicular to the other. Spiro compounds lack elements of symmetry and so exist in two non superimposable forms.



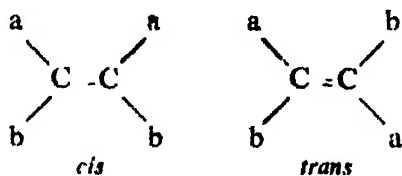
Spiro [3.3] heptan-2, 5-dicarboxylic acid

Certain types of bridged aromatic compounds as exemplified below also exhibit molecular asymmetry



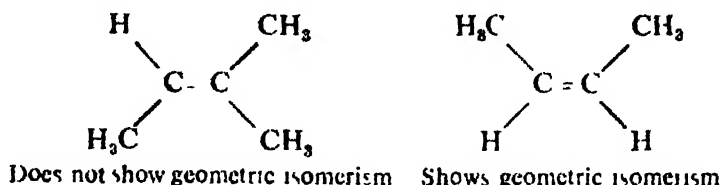
4.6 GEOMETRIC ISOMERISM

Geometric or *cis-trans* isomerism is a direct consequence of a high energy barrier to rotation at the double bond and is frequently encountered in unsaturated compounds. Groups around a carbon-carbon double bond can be arranged spatially to give two types of isomers called the *cis* (Latin-on the same side) and *trans* (Latin-across) as shown in the following structure:



The two forms have the same molecular formula but differ in configuration and are called *geometric isomers*. Presumably, a double bond alone is not sufficient to produce geometric isomers. Ethylene, 1, 1-dichloroethylene, etc.

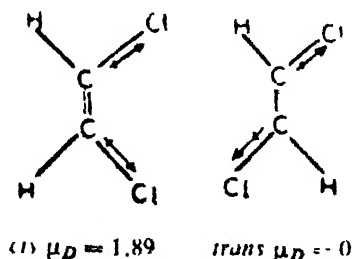
do not exhibit geometric isomerism. It is, therefore, necessary that the two groups attached to the carbon atom at one end of the double bond be different from one another and the two linked to the carbon atom at the other end of the bond also be different. This is illustrated by the following examples:



Geometric isomerism is also exhibited by compounds containing C-N bonds, N=N bonds and by cyclic compounds. Geometric isomers differ widely in their physical and chemical properties unlike enantiomers.

1. **Melting Point:** The *cis*- and *trans*-isomers have different melting points and boiling points. For instance, *cis*-1, 2-dibromoethylene melts at -53° while the *trans*-isomer at -6° .

2. **Dipole Moment:** The dipole moments of the isomers are quite different. Thus *cis*-1, 2-dichloroethylene has μ_D of 1.89 while the *trans* compound has a value of zero

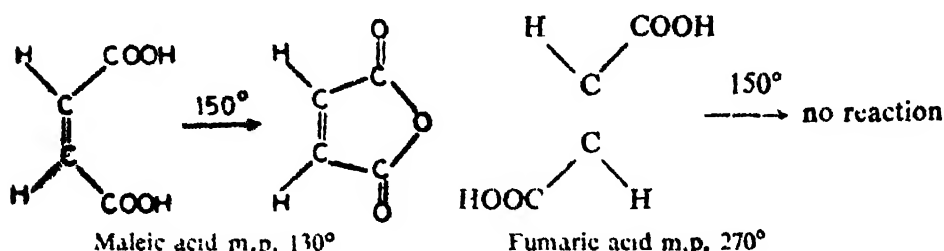


In the *cis*-isomer the individual bond moments are additive while in *trans* the vector sum is zero.

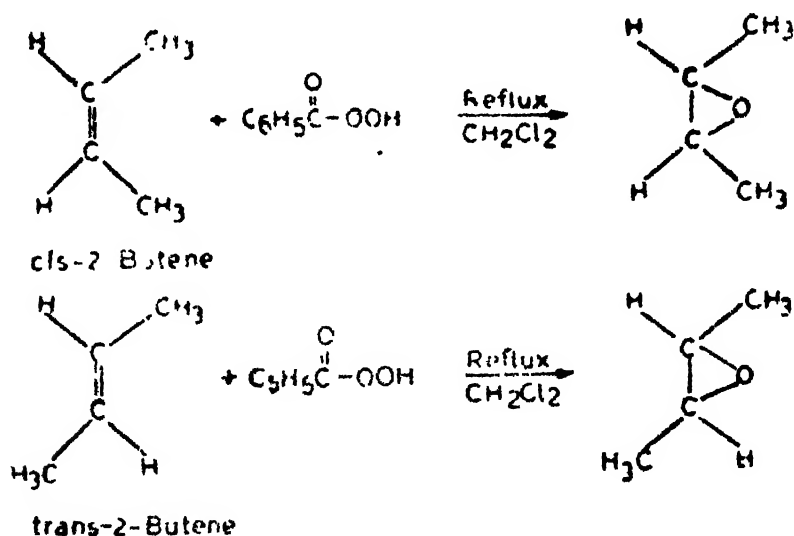
3. **Infrared Spectra:** A change in dipole moment is necessary for a compound to give rise to infrared absorption. In symmetrically substituted ethylenes, for instance stretching involves no change in the dipole moment and is thus infrared inactive. Thus a *trans*-isomer which possesses an element of symmetry i.e. a center of symmetry and a dipole moment equal to zero, does not show stretching of the double bond. The *cis*-isomer, on the other hand, shows a strong carbon-carbon double bond stretching frequency around 1590 cm^{-1} .

4. **Anhydride Formation:** A *cis*-dicarboxylic acid, on heating, loses a molecule of water and this leads to the formation of an anhydride. In a

cis-dicarboxylic acid, the two carboxyl groups are oriented on the same side, a water molecule can thus be lost with the formation of an anhydride. Maleic acid (*cis*) on heating at 150° loses water to form maleic anhydride. The *trans*-isomer, fumaric acid is recovered unchanged under these conditions

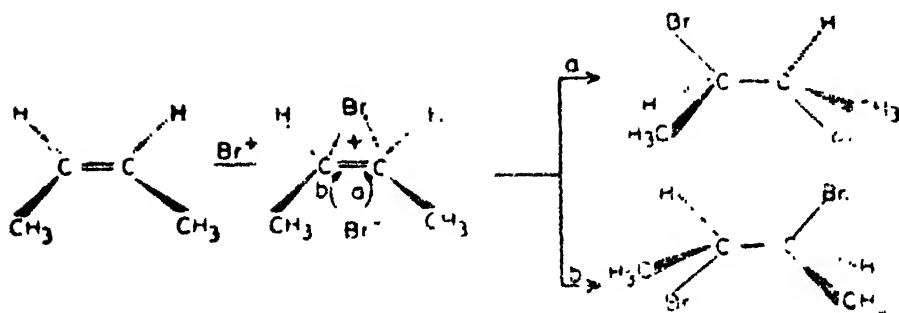
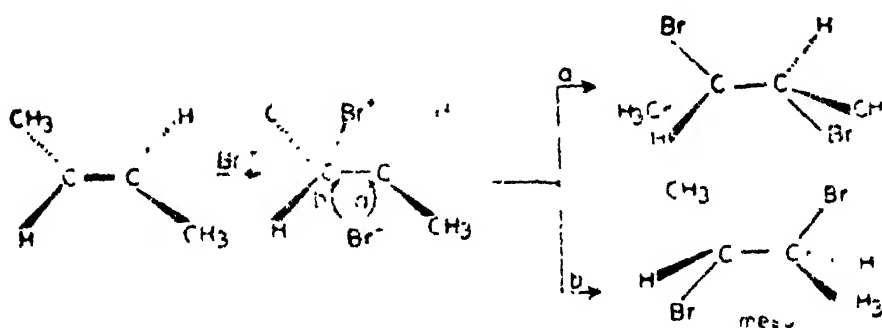


5. *Epoxide Formation*: Epoxidation is carried out by refluxing an olefinic compound with a peracid, such as perbenzoic acid in an inert solvent. This reagent adds in a *cis* manner. The *cis* olefin on epoxidation yields the *cis*-epoxide while a *trans*-epoxide is obtained from the *trans*-isomer:



The reaction thus proceeds in a stereospecific manner. Such reactions, in which the configuration of the groups is preserved in the products are called *stereospecific*.

6. *Electrophilic Addition*: The *cis*- and *trans*-alkenes behave differently towards the electrophilic addition of Cl_2 , Br_2 , etc. The halogenation takes place in a *trans* manner. The *cis*-isomer yields a (\pm)-pair, i.e. a racemic mixture while the *trans*-isomer yields a *meso* compound.

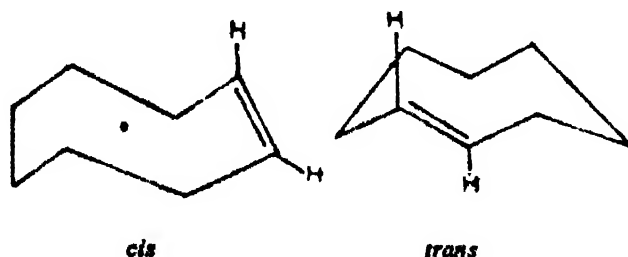
*cis*-2-Butene*d, l*-pair*trans*-2-Butene

meso

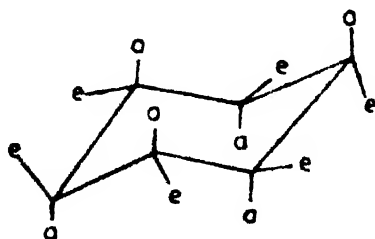
These two products are similar and contain a point of symmetry.

4.6.1 Geometric Isomerism in Cyclic Compounds

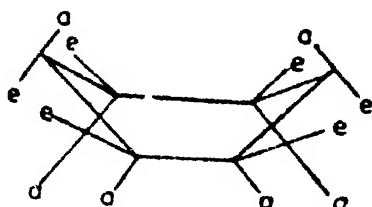
Geometric isomerism is also observed in ring compounds, as stated earlier. For the unsaturated ring systems only the *cis* forms of cyclopropene, cyclobutene, cyclopentene, cyclohexene and cycloheptene are known, since the *trans*-forms would be highly strained. However, both the *cis*- and *trans*-forms of cyclooctene and higher cycloalkenes are known. In these compounds a sufficient number of carbon atoms are present to allow folding of the methylene groups into a relatively unstrained conformation as illustrated below for cyclooctene:

*cis**trans*

In saturated cyclic compounds, the carbon atoms that form a single bond are tied together by the ring and there is no free rotation. Many of such rings are thus associated with optical activity. Three-membered rings are necessarily planar; substituted rings can, however, be arranged in *cis*- and *trans*-manner. Cyclobutane and cyclopentane adopt a non-planar conformation to reduce the eclipsing in the planar form. The cyclohexane ring has been extensively investigated and it has two stable non-planar forms. These are known as the *chair* (rigid) and the *boat* (flexible) cyclohexanes. The C-H bonds are classified into two types called the *axial* (a) and the *equatorial* (e). In the chair model the hydrogen atoms are as far apart as possible and this form is thus of lower energy. The boat-form, because of

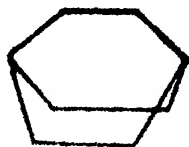


Chair form



Boat form

severe eclipsing of both adjacent and 1, 4-hydrogens, is of higher energy and is relatively less stable than the chair model. The boat form thus represents only a very small percentage of cyclohexane in an equilibrium mixture at room temperature. The energy difference between the two forms has been estimated to be of the order of 5.6 Kcal/mole. There are, nevertheless, some molecules in which the cyclohexane ring exists in the flexible form, bicyclo [2.2.2] octane represents such a case

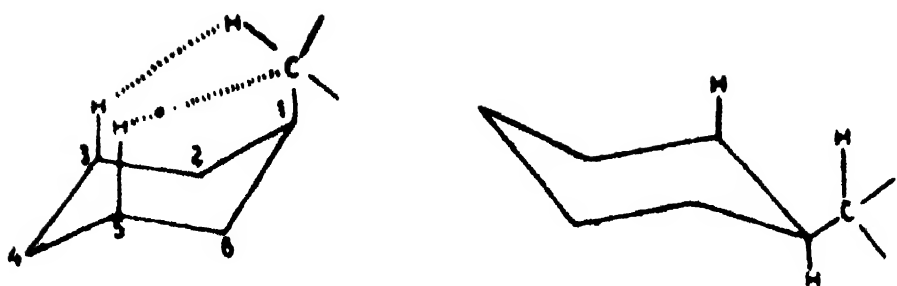


Another example in which the cyclohexane takes up a boat-shaped form is *trans*-1, 3-di *t*-butylcyclohexane.

The chair-form is the stable form only amongst small rings in which it is capable of taking up a strain-free conformation. There are two additional features of a cyclohexane ring

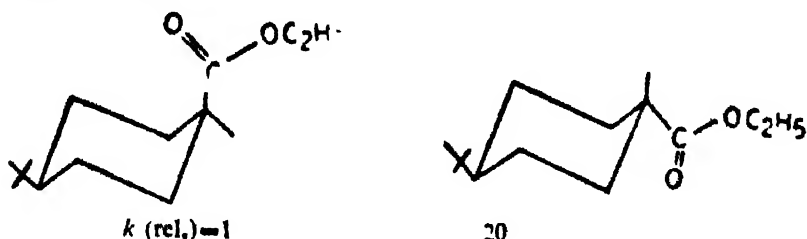
1. One chair form readily flips into the other and in the process the equatorial bonds become axial and *vice versa*.

2. Large groups tend to occupy equatorial rather than axial positions. Consider methyl cyclohexane. In one conformation, the $-\text{CH}_3$ group is axial and in the other, it is equatorial. These two conformations are energetically different because of the 1, 3- and 1, 5-interactions with the $-\text{CH}_3$



group in the first case while the other has none. The former is analogous to *gauche* arrangement while the latter is *anti*. The energy of the former is higher by 0.8 Kcal/mole and increases as the size of the group increases. Thus, *tert.* butyl group in *tert.* butyl cyclohexane lies exclusively in the equatorial conformation and is often called the 'anchoring' group.

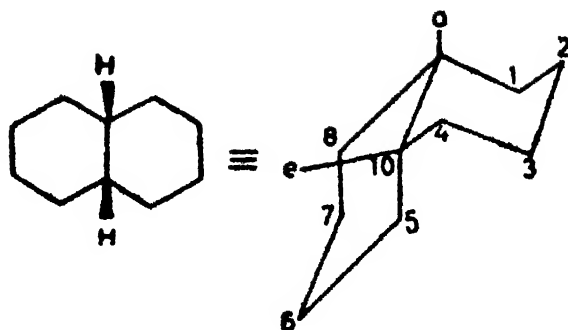
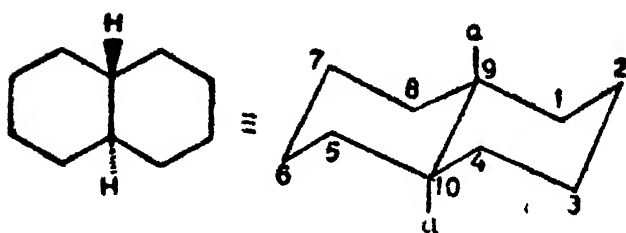
Chemical Reactivity. Barton first pointed out the chemical consequences of the differences between axial and equatorial substituents. The preference for a chair-form is merely due to the fact that this is the only way of obtaining the correct staggering in all C-C bonds. The difference in chemical behavior caused by the substituents placed in the axial and equatorial positions are due to steric factors. The axial position is normally hindered and the reaction proceeds more slowly than in the equatorial position. Thus, the saponification of carboxylic acid ester proceeds with marked retardation in the axial position.



Since hydrolysis proceeds *via* the formation of a tetrahedral intermediate in which the bulk increases, the axial saponification thus proceeds slowly.

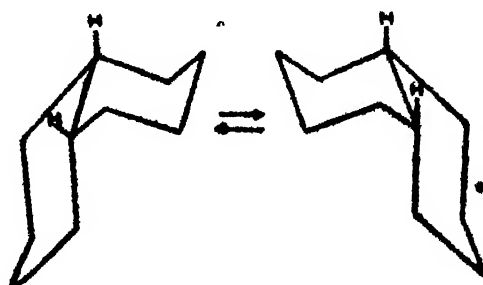
4.6.2 Bicyclic Alkanes

Ring systems can be fused through adjacent carbon atoms and are called condensed rings. The fusion can be either *cis* or *trans*. For small rings only *cis* fusion is possible. Many of the molecules that we come across in organic chemistry contain more than one ring. One such example is bicyclo [4.4.0] decane, a compound popularly known as decalin. It also exists in two geometric isomers, *cis*-decalin (b.p. 194°) and *trans*-decalin (b.p. 185°).

*cis* XXII*trans* XXIII

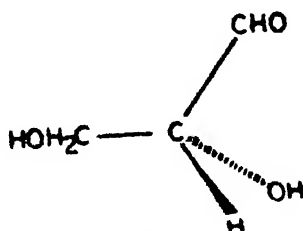
In the former, the fusion is through axial-equatorial bonds and in the latter through equatorial-equatorial bonds.

cis- and *trans*-Decalins cannot be interconverted into one another by simple rotation about the carbon-carbon single bond. These are thus isomeric and not different conformations of a single compound. Analogous to cyclohexane, *trans*-decalin has lower energy and is more stable. Moreover, diequatorial fusion of the ring (*trans*) renders the molecule more rigid, i.e. complete conversion of the molecule into a new chair conformation is impossible on the equatorial bonds at the junction carbon atoms cannot become axial unlike *trans*-1, 2-dimethylcyclohexane. The *cis*-compound, on the other hand, is more flexible and the interconversion of the axial and equatorial bonds is allowed as in the case of *cis*-1, 2-dimethylcyclohexane.



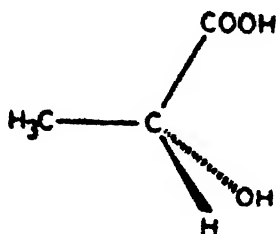
4.7 ABSOLUTE CONFIGURATION AND SPECIFICATION

Absolute configuration may be described as the orientation of groups in space relative to one another. Determination of absolute configuration is a cumbersome process and can be accomplished only if the compound forms well defined crystals. The configurations of a great many compounds are correlated with that of a known compound and what we actually determine is the *relative configuration*. The compound of reference for this purpose was selected to be D (+)-glyceraldehyde and the configuration of compounds that could be derived from D (+)-glyceraldehyde was considered to belong



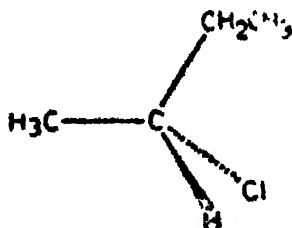
D (+)-Glyceraldehyde

to the D-family and those that resembled (L)(-)-glyceraldehyde to the L-family. On this basis, D-Lactic acid was assigned the following configuration:



D-Lactic acid

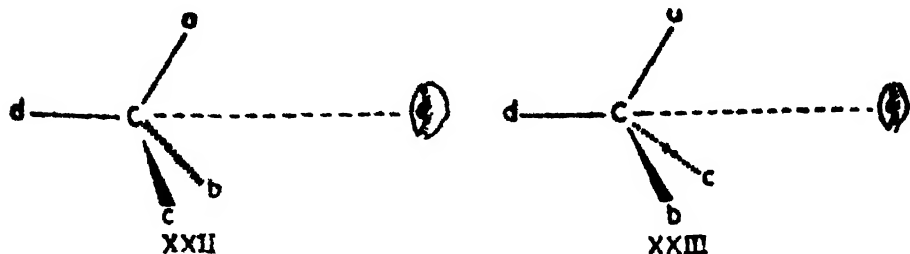
There is no difficulty in applying the D and L system of classifying enantiomers to lactic acid because the —COOH group corresponds to —CHO and —CH_3 group to $\text{—CH}_2\text{OH}$. The system, however, is less obvious with compounds like 2-chlorobutane because a comparison of groups with those present in D (+)-glyceraldehyde cannot be easily made.



2-Chlorobutane

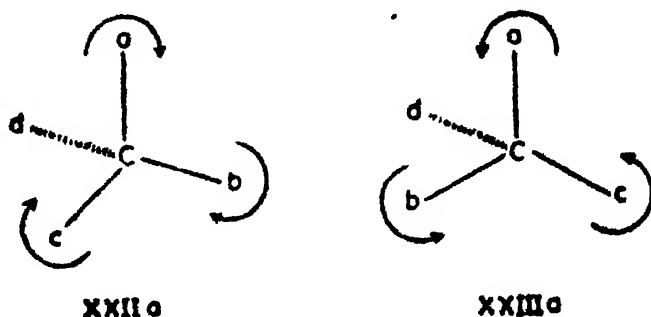
An independent system has been developed by *Cann, Ingold* and *Prelog* to name configuration without reference to glyceraldehyde. The new system is called the *R-S convention*. According to this, a relative sequence is assigned to substituents located on a carbon atom. The procedure involves the following steps:

1. Assign a sequence of priority to the atoms or groups attached to the asymmetric carbon atom. Let us consider a molecule *Cabcd* in which the space model is represented as in structure (XXII).



Let us also suppose that the order of priority of groups in terms of atomic number is *a b c d* where *d* is of lowest priority and is usually a hydrogen atom. Structure (XXIII), is an enantiomer of (XXII). An enantiomeric form can be written by interchanging the positions of any of the two groups.

2. Position the molecule in such a way that the atoms of lowest priority, i.e. *d*, points away from you (see corresponding models XXIIa and XXIIIa)



Now, view the model and determine whether in passing from *a* to *b* to *c*, a clockwise or an anticlockwise curve is traced. If the curve traced is clockwise then the asymmetric carbon atom is called *R* (*rectus*, right), and *S* (*sinister*, left) if the curve traced is anticlockwise. The *R* and *S* notations are also independent of the sign of rotation.

4.7.1 The Priority Rules

To decide the priorities of the groups attached to the central carbon, the following rules may be observed.

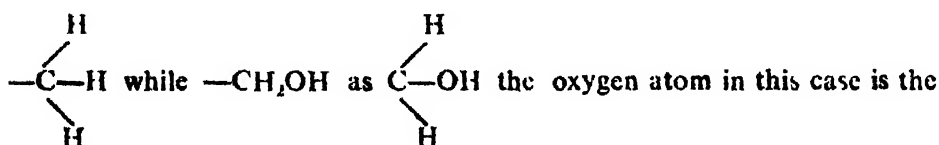
1. For the four different atoms or groups attached to the asymmetric carbon atom, the priority depends on the atomic number. An atom with higher atomic number precedes the lower, i.e.



2. In case two atoms are isotopes of each other, the heavier isotope has the higher priority, i.e.

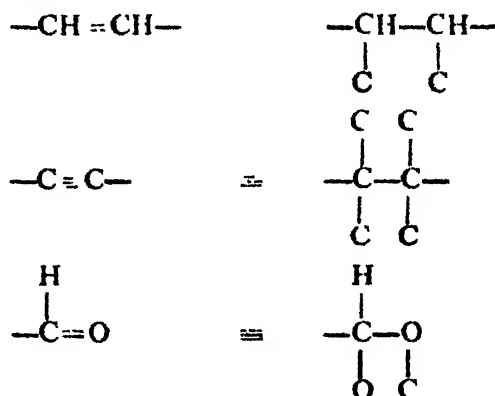


3. More often, in organic chemistry, two or more atoms directly linked to the asymmetric center are identical. In that case work outwards along the chain till the priority is determined. For instance, between $-\text{CH}_3$ and $-\text{CH}_2\text{OH}$, the latter has a higher priority because $-\text{CH}_2\text{OH}$ can be written as

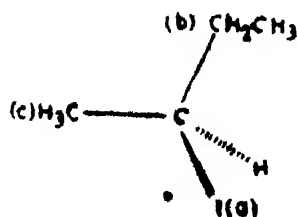


deciding factor.

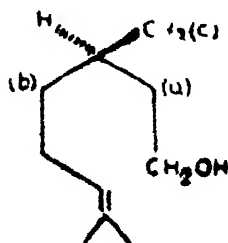
4. A double bond to an atom is considered equivalent to two such atoms and a triple bond equivalent to three. The bonded atoms are thus considered as follows



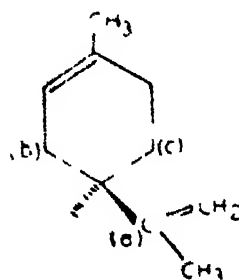
The following examples illustrate these rules:



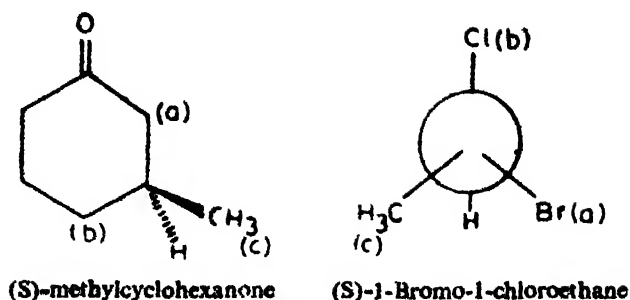
S (+)-2-iodooctane



R (+)-citronellal



R (+)-limonene

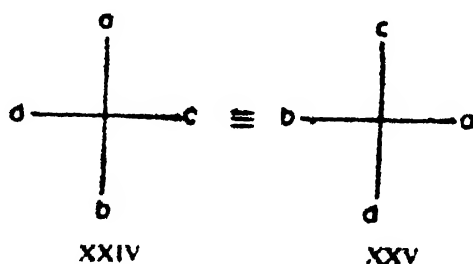


(S)-methylcyclohexanone

(S)-1-bromo-1-chloroethane

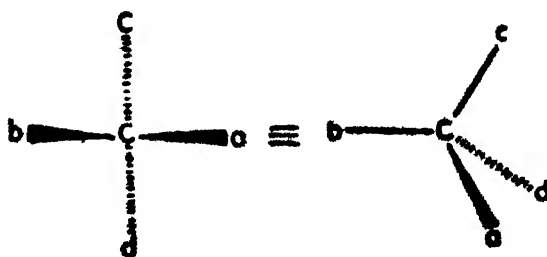
The usual *Fischer projection* can be handled easily after it is translated into a three dimensional representation. Alternatively a procedure which does not require three dimensional thinking is as follows:

Transform the given *Fischer projection* by an even number of interchanges of pairs of substituents so that the group of lowest priority, i.e. *d* occupies the bottom position. On this structure read the pattern $a \rightarrow b \rightarrow c$ as R or S depending upon whether the direction of movement is clockwise or anti-clockwise. If group *d* is already at the bottom in the given projection, then no exchange is needed. This is illustrated for the following general case:



XXIV

XXV



XXVI

The two structures (XXIV) and (XXV) are equivalent because an even interchange of groups does not alter the configuration. The new structure (XXV) traces a clockwise curve, so its configuration is R. Interchanging of one pair of groups would reverse the configuration.

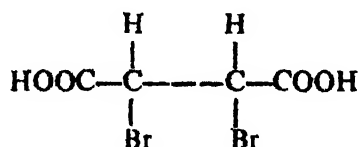
QUESTIONS

4.1 Describe the following terms:

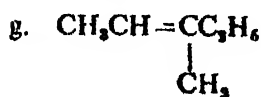
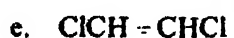
Diastereoisomer, resolution, dissymmetry, racemization, absolute and relative configurations.

4.2 a. Describe optical isomerism with suitable examples.

b. Would you expect the following compounds to be optically active? Explain.



4.3 Indicate the possible types of isomerism exhibited by the following compounds



4.4 Which of the following structures exhibit *cis-trans*-isomerism?

a. 2-Methyl-2-pentene

b. 3-Methyl-3-pentene

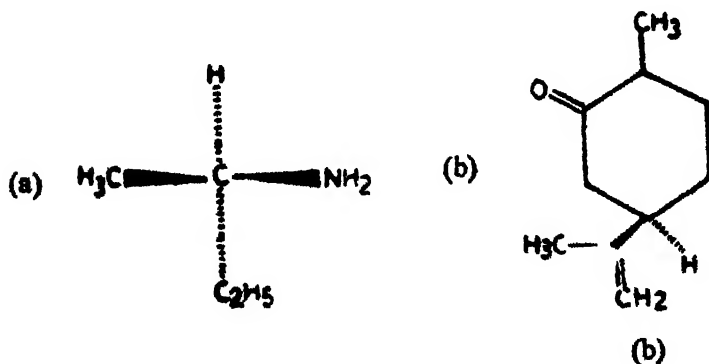
c. 1, 2-Dimethylcyclohexane

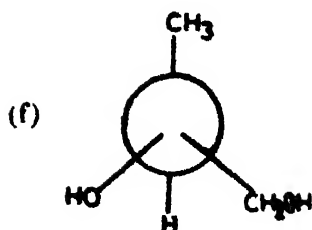
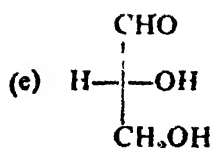
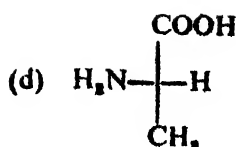
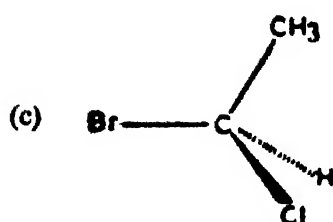
d. Cyclohexene

e. 2-Hexene

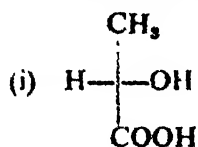
4.5 Which of the following compounds is not isomeric with diethyl ether: Butan-1-ol, butanone, 2-methylpropan-2-ol and *n*-propyl methyl ether.

4.6 Write R/S configuration for the following compounds.

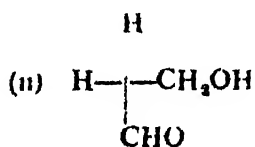
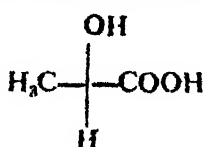




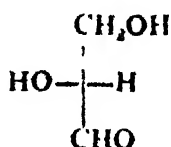
- 4.7 (a) Describe the rules for interchanging *Fischer projection* into an equivalent structure.
 (b) Show the relationship between the following pairs.



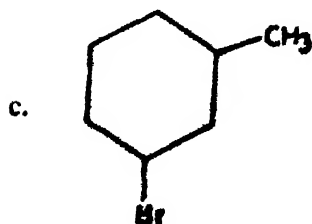
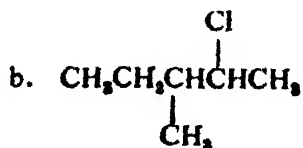
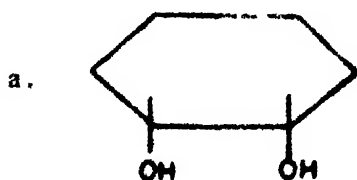
and

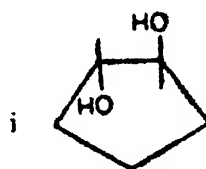
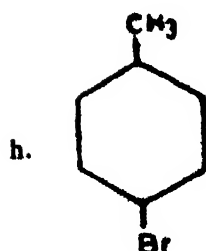
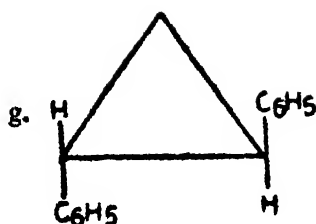
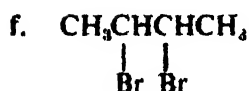
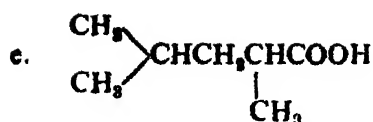


and



- 4.8 How many optically active forms are possible for the following compounds?

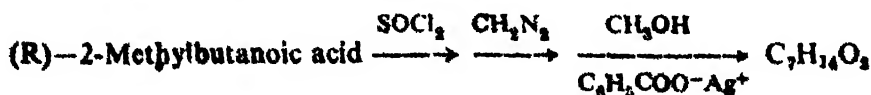




4.9 Indicate whether the following statements are true or false

- R and S configurations correspond to the enantiomers of an optically active compound.
- The process of converting an optically active compound into a racemate is called racemization.
- Cyclic disubstituted compounds do not show geometric isomerism.
- A molecule containing a plane of symmetry can be optically active.
- Positional and chain isomerism are identical.
- Optical isomers that are not enantiomers are called diastereoisomers.
- All *ortho* substituted diphenyl compounds are optically active.
- In the *Fischer projection*, any odd number of interchanges of substituents leads to an enantiomer.
- All chiral objects are asymmetric.

4.10 Predict the structure and stereochemistry of the product from the following sequence of chemical reactions:



4.11 By drawing Newman projection formulas, show how do the potential energy changes occur in *n*-butane when the molecule is rotated around its $\text{C}_2\text{—C}_3$ bond axis through a complete cycle.

- 4.12 Give an account of the isomerism exhibited by lactic acid. What is meant by resolution? Describe at least two methods for resolving a racemic compound.
- 4.13 What do you understand by the term optical activity? Explain it with reference to lactic and tartaric acids.
- 4.14 Discuss the different types of isomerism. Illustrate each with an example.
- 4.15 What do you know about dissymmetry, an essential condition for optical isomerism?
- 4.16 What do you understand by the terms R and S used for specifying the configuration of optically active compound? Do they throw any light on the direction of rotation of the compound?
- 4.17 (a) Is geometric isomerism possible in compounds which contain (i) Two double bonds (ii) No double bond? Give reasons. How can maleic acid be converted into tartaric acid? Give structures of crotonic acid and its other geometric isomer.
- (b) Solution of optically active compounds showing positive rotation are called *dextro* and the ones showing negative rotation are called *levo*. Can these be denoted as D and L respectively? Give reasons for your answer.
- (c) What is 'meso' form? How does it differ from racemic form?
- 4.18 How will you resolve racemic lactic acid into optically active form?
- 4.19 What is meant by stereochemistry? Discuss optical isomerism of lactic acid.
- 4.20 a. What are R and S configurations? State and illustrate the sequence rules.
- b. Write an account of the properties of enantiomers.
- 4.21 What do you know about the chair and boat forms of cyclohexane?
- 4.22 Which of the following compounds will exhibit optical isomerism?



5

Reaction Intermediates and Mechanisms

Organic compounds undergo a large variety of interesting reactions and their study has been facilitated by investigating their mechanisms. A *mechanism* may be described as the detailed description of the sequence of steps in going from the reactants to the products. A reaction is conveniently represented by a stoichiometric equation which provides a knowledge about the nature of the reaction but tells nothing about its mechanism. Several techniques, both kinetic and chemical, are employed in organic chemistry to delineate the mechanism of a reaction under examination. Organic reactions can be broadly classified into the following types :

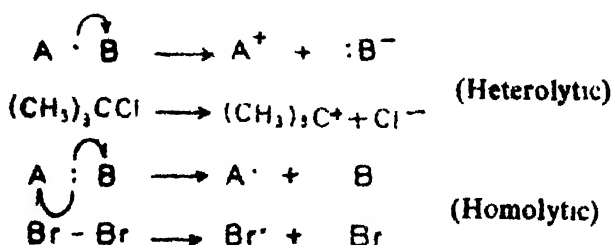
Reaction type	Overall transformation
1. Substitution:	$\text{CH}_3\text{Br} + \text{OH}^- \longrightarrow \text{CH}_3\text{OH} + \text{Br}^-$
2. Elimination.	$\text{CH}_3\text{CH}_2\text{CH}_2\text{OH} \xrightarrow{\text{H}^+} \text{CH}_3\text{CH}=\text{CH}_2 + \text{H}_2\text{O}$
3. Addition to C=C bond:	$\text{H}_2\text{C}=\text{CH}_2 + \text{Cl}_2 \longrightarrow \text{ClCH}_2\text{CH}_2\text{Cl}$
4. Radical reaction.	$\text{CH}_3\text{CH}_3 + \text{Cl}_2 \xrightarrow{h\nu} \text{CH}_3\text{CH}_2\text{Cl} + \text{HCl}$
5. Rearrangement:	$ \begin{array}{ccc} \text{C}_6\text{H}_5 & & \text{OH} \\ & \diagdown & / \\ & \text{C} & \text{N} \\ & / & \diagdown \\ \text{C}_6\text{H}_5 & & \end{array} \xrightarrow{\text{H}^+} \begin{array}{ccc} & & \text{O} \\ & & \\ \text{C}_6\text{H}_5 & \text{CNHC} & \text{C}_6\text{H}_5 \end{array} $

Formation of CH_3OH from CH_3Br in the presence of a nucleophile (OH^-) is a substitution or displacement reaction in which the bromide ion has been displaced by hydroxide ion. Removal of water from propanol in an acidic medium with the formation of propene is an elimination process. Addition of chlorine to ethylene leading to the formation of 1,2-dichloroethane is an example of a carbon-carbon double bond addition. In radical

reactions, the intermediate formation of radicals and the subsequent formation of the product takes place in the presence of light. An atom or group migrates from one position to another in molecule, in a rearrangement reaction. Above reaction is an example of the familiar Beckmann rearrangement.

5.1 BOND FISSION

Organic reactions proceed by the cleavage of covalent bonds. A cleavage or fission can take place in either of two ways, i.e. *heterolytic*, in which the fragments separate and one fragment retains the shared pair of electrons, and, *homolytic*, in which each fragment separates with a single unpaired electron each.



Bond fission results in the formation of intermediates.

5.2 REACTION INTERMEDIATES

In the study of organic reactions, energy as a parameter is of fundamental importance. Of particular interest is the *activation energy*, described as the minimum energy required for a reaction to take place. The energy of

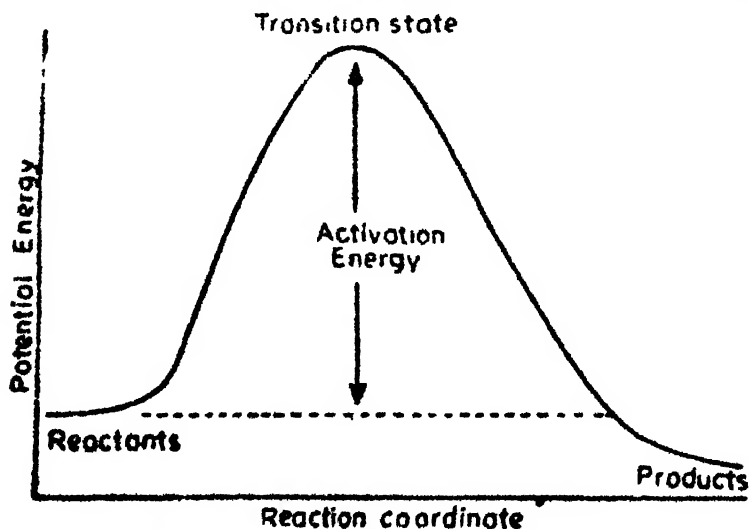


Fig. 5.1 Potential Energy Diagram

*The curved arrow represents the transfer of both the electrons to one atom while the fish hook implies transfer of one electron only.

a reaction *versus* the progress of the reaction is plotted on a diagram known as the *potential energy diagram*. The progress of the reaction is expressed as *reaction coordinate* and is measured in terms of bond breaking and bond making. A potential energy diagram for a typical reaction is shown in Fig. 5.1. The transition state is energetically the highest point above the reactions *en route* to the products. It represents a state in which the reactant bonds are partially broken and the bonds in the products are partially formed. It lies on the energy maxima on the potential energy diagram. It has an extremely brief existence. The structure of the transition state is an important feature of a reaction and its existence is deduced by indirect means. A molecule in the transition state is called an *activated complex*. The activation energy is thus the energy required in taking the reactant to the transition state. The higher the transition state above the reactants, the slower is the rate of the reaction because the necessary energy is less likely to be available to the reactants to cross the activation barrier. Conversely, the rate is faster if the transition state is lower. In addition, if the transition state is more stabilized by some structural features, than the reactants, the energy barrier is reduced. On the other hand, if the transition state is destabilized then the energy is larger and the rate of formation of products is decreased.

A reaction intermediate is a transient species formed during a reaction and corresponds to an energy minimum on the potential energy diagram (Fig. 5.2).

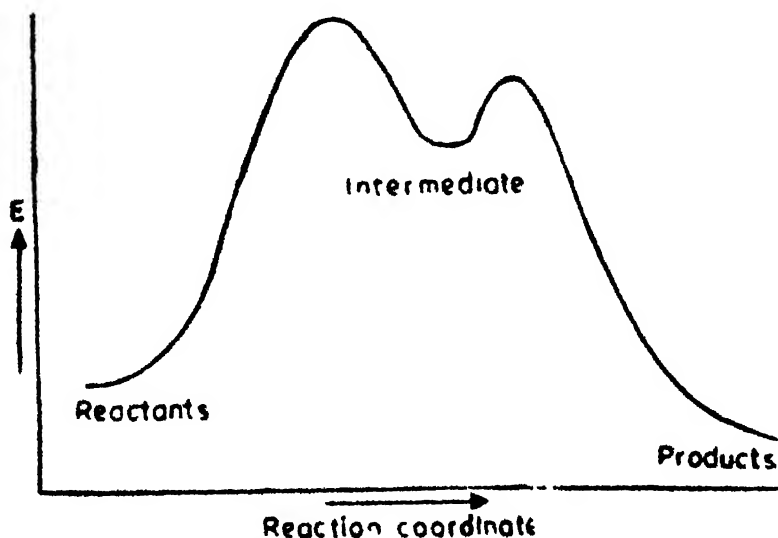


Fig. 5.2 Representation of a Reaction Intermediate

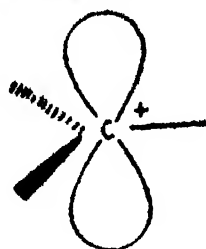
Figure 5.1 represents the energy diagram for the simplest possible reaction in which there is a single transition state. In more complicated cases, there is an additional transition state and intermediate energy minimum, i.e., the intermediate and the highest of the two determines, the activation energy

of the reaction. This step of highest energy of the overall reaction proceeds more slowly than any other and also governs the rate of the reaction and is called the *rate determining step*.

A vast majority of organic reactions take place *via* the formation of intermediates. These may be either charged or neutral species, but all are shortlived and very reactive. Different intermediates differ widely in stability.

5.2.1 The Carbocations

An ion with a positively charged carbon atom is called a *carbocation*. In a carbocation, the carbon atom has six electrons and is thus deficient in electrons. The central carbon atom is sp^3 hybridized and the three bonds attached to it are planar. The remaining p -orbital is empty.

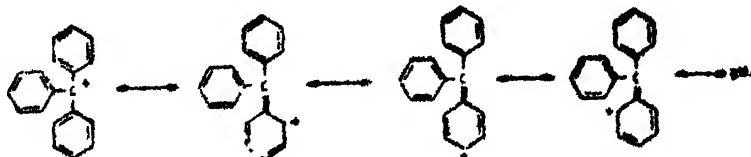


empty p -orbital

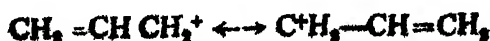
A carbocation can be generated in a number of ways. Its formation is favoured in polar solvents. The ion may be obtained by the heterolysis of an organic halide in a polar solvent, deamination of amines, protonation of alcohols and in the Friedel-Crafts reaction.

Carbocations differ in stability depending on the nature of the groups attached to the positively charged carbon atom. The order of stability can be predicted conveniently by invoking either resonance or inductive effect. The order of stability of the carbocations increases in the following

manner: $C_6H_5CH_2^+ < C_6H_5\overset{+}{C}HCH_3 < (C_6H_5)_2\overset{+}{C}H < (C_6H_5)_3\overset{+}{C}$. The triphenylmethyl carbocation is the most stable in this series because its positive charge is dispersed by resonance with the resultant stability of this ion.

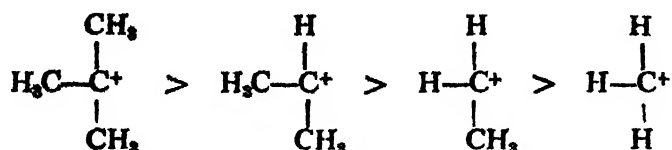


An allyl cation is similarly stabilized by resonance:



If the alkyl groups are attached to the carbon atom then a tertiary alkyl

carbocation is more stable than a secondary which in turn is more stable than a primary due to a favourable inductive electron-donating effect.



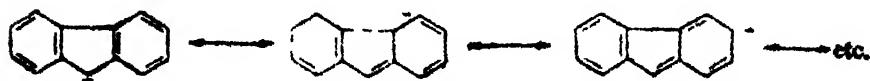
A carbocation is an electron deficient species and in this case there can be no occurrence of resonance, therefore, the charge is dispersed by inductive electron-donating effect of the alkyl groups.

5.2.2 The Carbanions

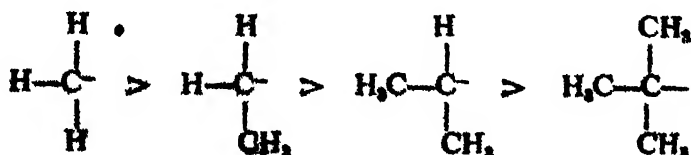
An ion with a negatively charged carbon atom is called a *carbanion*. The carbon atom in a carbanion is trivalent and has two extra electrons which are not bonded. A carbanion is isoelectronic with an amine and is sp^3 hybridized. The unpaired electron pair forms the fourth apex of the tetrahedron. The configuration of simple carbanions seems to be pyramidal



which readily oscillates from one side of the plane to the other. Carbanions can be generated by a number of methods, such as removal of a proton from hydrocarbons by strong bases, removal of a proton from an activated methylene group and in the Grignard reaction. A carbanion is stabilized by resonance, and is shown for the fluorenyl anion.

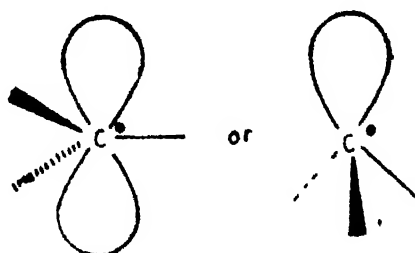


In contrast to alkyl carbocations the order of stability of alkyl carbanions is reverse i.e., primary carbanion is more stable than a secondary or tertiary. The inductive electron-donating effect of the methyl groups tends to destabilize the tertiary carbanion.



5.2.3 The Free Radicals

A free radical has an unpaired electron (a total of seven as compared to eight in a carbanion) at the central carbon atom. It is uncharged but is still considered deficient in electrons. There are two possible structures for simple alkyl radicals, i.e. it may be planar sp^2 hybridized similar to a carbocation or as a pyramidal which is neither planar nor tetrahedral. Free



radicals are formed mainly in non-polar solvents. They are produced by homolytic cleavage of a bond. In photochemical processes the energy ($h\nu$) is frequently provided by u.v. light or the sun. Thermolysis of peroxides produces free radicals.

A free radical is stabilized by resonance analogous to a carbocation or carbanion, and the resonance structures for benzyl radical shown. The stability of alkyl free radicals parallels that of carbocations.



It may be stated that the resonance effects are always more stabilizing than the inductive effects. Between the following two carbocations

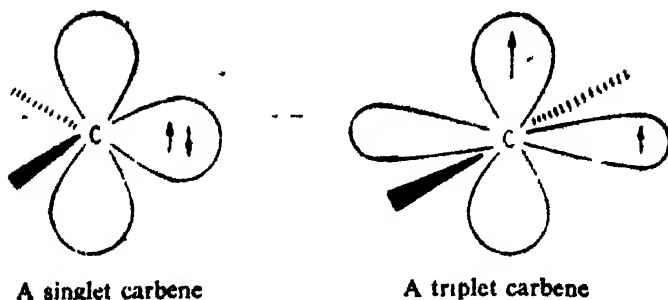
$C_6H_5\dot{C}HC_6H_5$ and $C_6H_5\dot{C}HCH_3$, the former is more stable because it has more resonance structures.

5.2.4 The Carbenes

There is yet another class of intermediates, the divalent carbon compounds

known as carbenes $\left(\begin{array}{c} R \\ \diagup \\ :C \\ \diagdown \\ R \end{array} \right)$. The central carbon atom has six electrons,

two of which are free. Carbenes do not possess any charge. Carbenes can exist in two forms, i.e. singlet and triplet. In *singlet carbene* the two non-bonded electrons are in the same orbital and paired. The two electrons in a *triplet carbene* are placed in each p_x and p_y orbitals and it is linear.



Carbenes may be generated by the thermal or photochemical decomposition of diazo compounds, decomposition of ketenes, action of strong bases on alkyl halides and decomposition of ylides. Depending on the mode of its formation, a carbene may initially be formed as singlet or triplet. The singlet state of methylene resembles a carbocation while the triplet state a diradical. One of the most important reactions of carbenes is their addition to an alkene to yield a cyclopropane.

5.3 CLASSIFICATION OF REAGENTS

Chemical reagents have been classified into types namely electrophiles and nucleophiles

Electrophiles: Electrophiles (Greek: electron loving) or electron seeking are those reagents that are positively charged, for example, NO_2^+ , Br^+ , Cl^+ , H_3O^+ , RN_3^+ , Ag^+ , CH_3CH_2^+ or contain an electron deficient atom such as S in SO_3 or SOCl_2 .

Nucleophiles: Nucleophiles (Greek: nucleus loving) or electron repelling are those reagents that are negatively charged, for example, OCH_3^- , OH^- , OC_2H_5^- , CN^- , H^- , $-\text{CH}_3\text{CO}$ or possess an electron rich atom, i.e., O in $\text{H}_2\ddot{\text{O}}$ or N in $\ddot{\text{N}}\text{H}_3$ and pyridine.

5.4 EQUILIBRIUM AND KINETICS

A chemical reaction may proceed in a single direction to completion, but in general it often takes place both in the forward and reverse directions. In the latter case, a thermodynamic equilibrium is established, i.e. the reaction is complete, when the products and reactants are present in indefinite concentrations. A thermodynamic parameter of major utility is the free energy, symbolized by F . In organic chemistry we often talk of the energy content of a substance or system which can be understood in terms of free energy. This parameter refers to the stability of a substance or a system. A system reacts in order to attain a state of lower free energy content. Sodium chloride, for instance, dissolves in water because the solution possesses lower free energy than salt and water individually.

Broadly speaking, a reaction proceeds rapidly when the products happen to have a low energy content than the reactants. The energy cannot be measured experimentally, rather it is the change in free energy (ΔF) of a reaction that can be determined. For the following equilibrium between A and B, the change in energy is expressed by equation (5.1).



It is the difference between the free energy contents of the

$$\Delta F = F_B - F_A \quad (5.1)$$

products and the reactants. The equilibrium constant K is given by $K = \frac{[B]}{[A]}$ where $[A]$ and $[B]$ are the molar equilibrium concentrations and this is related to the change in free energy in the following manner (equation 5.2).

$$\Delta F = -RT \ln K \quad (5.2)$$

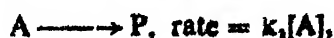
A reaction is considered to be spontaneous if ΔF has a negative value, this is considered to be the *driving force* for the reaction. If the change in free energy is zero then the system is at equilibrium.

The change in free energy can be broken up into two terms, ΔH (change in enthalpy) and ΔS (change in entropy) which are related as follows:

$$\Delta F = \Delta H - T\Delta S \quad (5.3)$$

where T is the temperature of the system.

The *enthalpy* term is generally associated with bonding. If stronger bonds are formed, ΔH is negative and the reaction is termed *exothermic*, a reaction in which ΔH is positive is *endothermic*. Entropy is concerned with the randomness of a system or the freedom of the reactants. A greater freedom for the reactants ensures a rapid reaction and a relatively positive change in ΔS . Thermodynamics deals with the initial and the final states of a system. It does not tell how the final equilibrium state was achieved and how fast this was attained. Chemical kinetics provides us with an answer for this last question as it deals with the change in the concentration of the reactants and products with time. Measurements of the kinetics of a reaction is the first step in the investigation of a reaction mechanism. It helps to establish the order of the reaction and the slow step of the reaction as well as the relative reactivities of molecules. The reaction rate is proportional to the concentration of the reactants and the proportionality constant is referred to as the *rate constant*. A reaction in which the rate of the reaction is proportional to the concentration of only one of the reacting substances, is termed as a *first order reaction*. The order of a reaction is the sum of the exponents of all the concentration terms which appear in the rate law.



where k_1 is the rate constant. The molecularity of a reaction is the number

of molecules involved in the actual collision process. The stoichiometric equation of a reaction corresponds to the *molecularity* for a simple reaction. A reaction is classified as a *second order* reaction, if the rate is proportional to the concentration of two substances. The rate for a reaction $A + B \longrightarrow P$ is given by

$$\text{rate} = k_2[A][B]$$

where k_2 is the rate constant for the second order reaction.

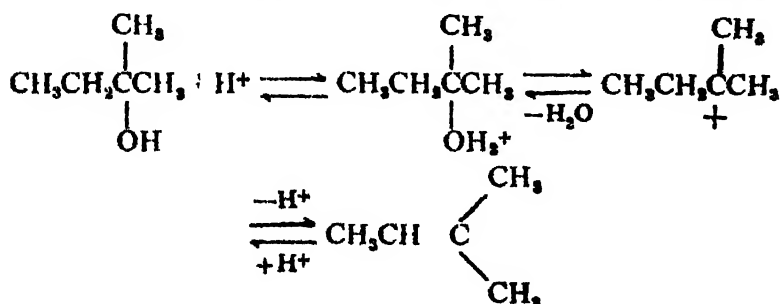
A rate law is obtained experimentally by measuring the rate of the reaction. The various mechanisms are written for the reaction and the one which corresponds to the experimentally determined rate equation and other data is considered to be the most plausible mechanism.

5.5 CHEMICAL METHODS FOR INVESTIGATING REACTION MECHANISMS

In addition to the information furnished by kinetics, certain chemical methods are employed in organic chemistry in order to confirm a postulated mechanism. Some of these techniques, namely product analysis, intermediate criteria, stereochemical studies and isotope labelling will be described here briefly.

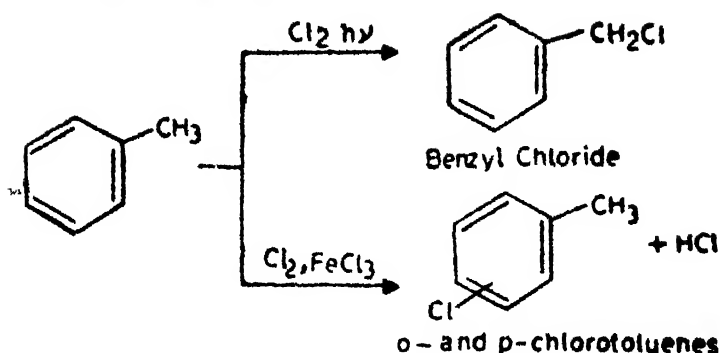
5.5.1 Product Analysis

The most obvious starting point in any mechanistic study is to identify the products of the reaction. The correct structure may be established by such techniques as ir, nmr, uv, ms, etc. To demonstrate this point let us consider a simple case of 2-methyl-2-butanol which is heated at 90° in the presence of dilute sulfuric acid. A careful analysis of the products indicates that the olefinic product, 2-methyl-2-butene is obtained in about 85% yield with the elimination of the elements of water. The mechanism of this dehydration can probably be thought of as proceeding *via* protonation of the alcohol as the first step. Subsequently a water molecule is lost resulting in

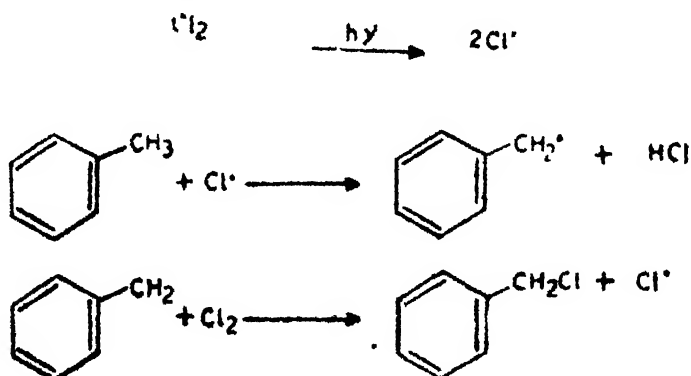


the formation of an intermediate carbonium ion. A proton is then lost to the solvent and preferably from the ethyl group, to yield the alkene.

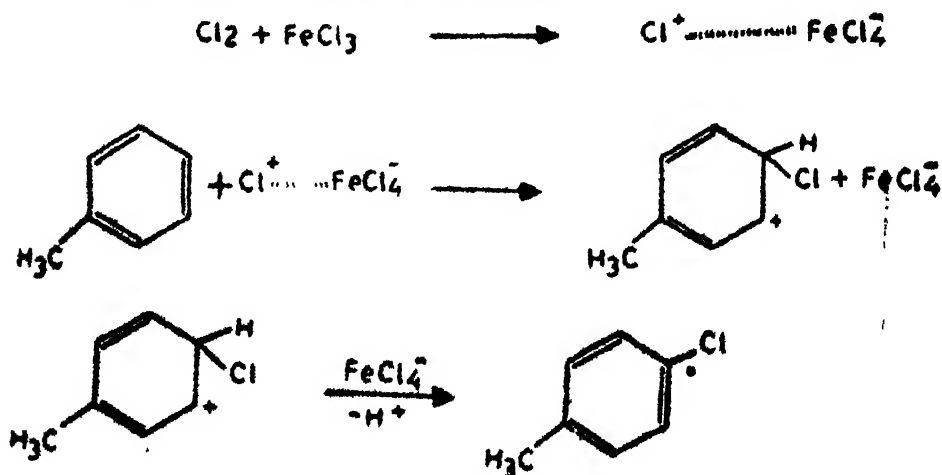
Another interesting example is the chlorination of toluene in uv light and under the catalytic effect of a Lewis acid (FeCl_3). Two different products are formed, as shown below:



The formation of these products immediately suggests a change in the mechanism during chlorination of toluene under two different conditions. In photochlorination, since the chlorine has not taken a position in the benzene ring, it is suggested that the reaction proceeds *via* a free radical mechanism involving the following steps:

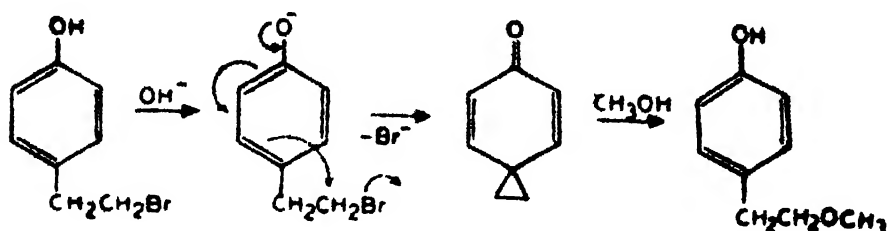


The Lewis acid-catalyzed reaction is the familiar electrophilic aromatic substitution in which an electrophile (Cl^+) attacks the aromatic ring with the subsequent loss of a proton to yield the products. *o*-Chlorotoluene is also formed in this reaction by a similar mechanism.

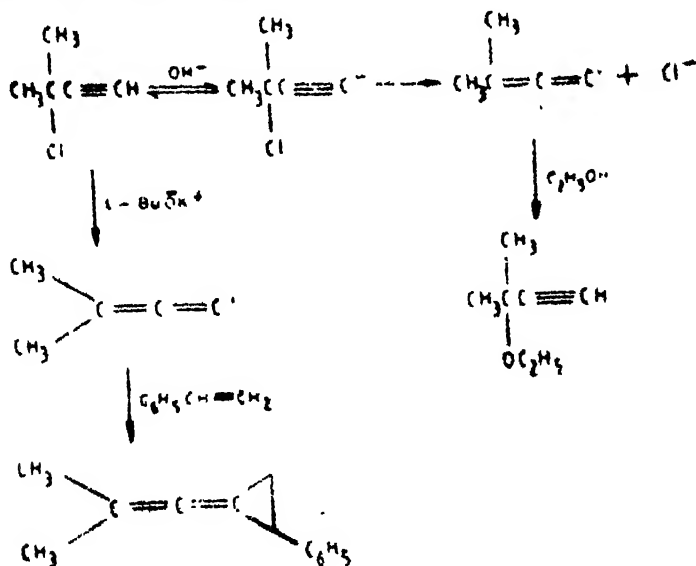


5.5.2 Intermediate Criteria

Intermediates are short-lived and very reactive species. A large number of reactions, however, proceed through intermediates of sufficient stability. An appropriate example is the solvolysis of *p*-hydroxyphenylethyl bromide in the presence of a base in methanol to form an ether. It was suggested that the reaction involves a spirodienone as an intermediate according to the



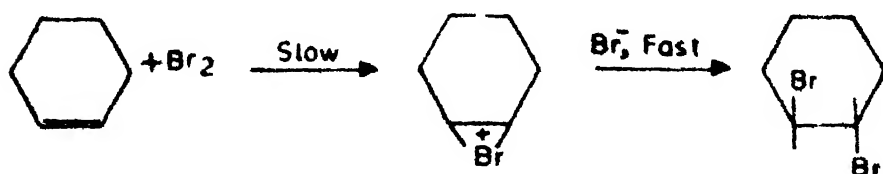
steps shown. The formation of this intermediate has been supported by actually isolating this intermediate. This intermediate, on subjecting to the above reaction conditions, yields the same product. If the intermediate is not isolable, its formation can often be demonstrated in a reaction by capturing it by a suitable reagent. For instance, in the solvolysis of 3-chloro-3-methyl-1-butyne in an alcoholic solution of potassium hydroxide, it was suspected that the reaction takes place through a carbene intermediate as follows:



A carbene is formed first by the loss of a proton and then the loss of the chloride ion. This was corroborated by doing the solvolysis in the presence of pot. *t*-butoxide and styrene. Under these conditions, the carbene, if formed, should be trapped by the olefinic double bond of styrene to form a cyclopropane derivative as carbenes are trapped by alkenes. An appreciable amount of this adduct was indeed obtained.

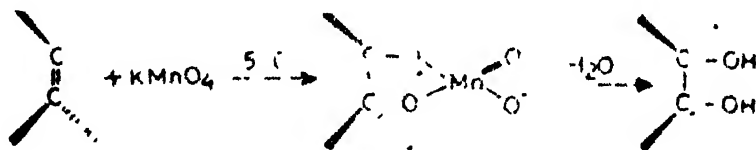
5.5.3 Stereochemical Studies

The contribution of stereochemical effects in elucidating reaction mechanisms has been particularly useful in several types of reactions. For this method to be useful, the stereochemistry of the reactants and products should be known accurately. The purpose is to determine a change in the configuration, or lack of it during the course of a reaction. Thus, the addition of bromine to cyclohexene is found to yield *trans*-1, 2-dibromocyclohexane as the predominant product. This implies that the reaction proceeds *via trans* addition and a cyclic 'bromonium ion' is involved. Subsequently, a bromide ion



the side opposite to the first bromine leading to the formation of a *trans* addition product. If a classical carbonium ion were involved then both *cis* and *trans* dibromocyclohexanes would have been obtained.

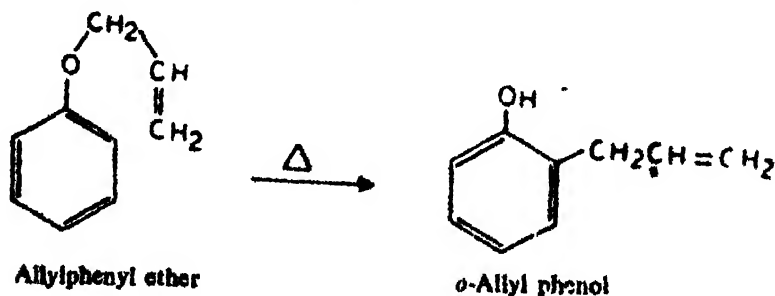
Hydroxylation of a carbon-carbon double bond by potassium permanganate or osmium tetroxide forms a 1, 2-*cis*-diol. The mechanism of this reaction may be interpreted by a *cis*-addition in which both the hydroxyl



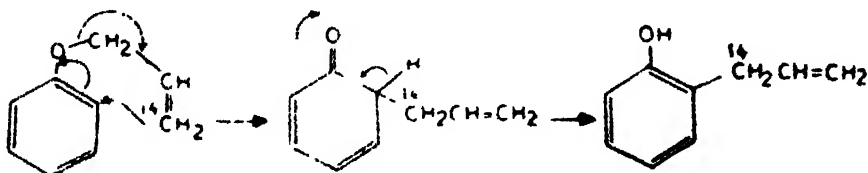
group add from the same side of the double bond, in contrast to bromine addition.

5.5.4 Isotope Labelling

This tool of diagnosing a reaction mechanism has been made possible by the availability of stable isotopes of various elements. The isotope effect is evaluated either by product analysis or kinetically. In the former case, one of the atom in the starting material is labelled and at the end of the reaction,

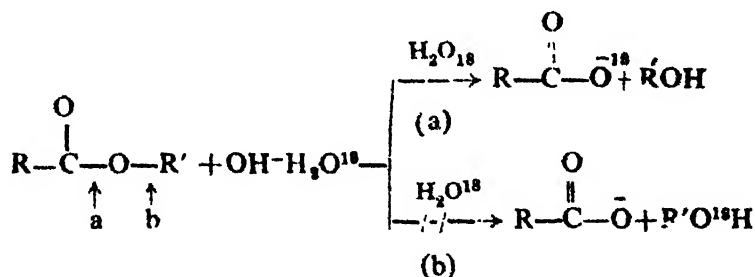


the identity of the product is established. The fate of the labelled atom is determined at the end of the reaction. A revealing example of isotope labelling study is the *Claisen rearrangement* in which phenyl allyl ethers on heating arrange to allyl phenols. Two mechanisms can be envisaged for this reaction. The first is a two step process in which a cleavage of the O—C bond takes place to give two fragments which recombine subsequently to form the product. The second is a concerted process in which bond-breaking and bond-making takes place simultaneously as shown below:



The distinction between the two pathways has been made by labelling the terminal carbon atom with C^{14} , and in the product it was always found to be adjacent to the aromatic ring. Therefore, a concerted process is more likely for this reaction, since according to the first mechanism, there would only be a 50 percent chance of the labelled carbon getting attached to the aromatic ring.

Another interesting problem which isotope studies have helped to solve is the alkaline hydrolysis of esters. In ester hydrolysis an acid and alcohol can be obtained either by acyl-oxygen fission (path a) or by alkyl-oxygen fission (path b). To decide between these two modes of fissions, the



reaction was run in water labelled with $O^{18}(H_2O^{18})$ and the product analyzed for the incorporation of oxygen-18. It was found that carboxylic acid and not the alcohol was enriched in oxygen-18. This conclusively demonstrated that acyl-oxygen fission (path a) took place and not path b.

Kinetic Isotope Effect: Isotope labelling has been a vital source of information for the elucidation of reaction mechanisms. Isotope effects can also be evaluated kinetically in reactions which involve the fission of a C—H bond. This method tells us whether a C—H bond is broken in the slow-step of the reaction or not. To do this, the rate K_M is measured with

the compound itself (for instance nitration of benzene) and then K_D is measured using the deuterated compound. The *kinetic isotope effect* referred to as K_H/K_D is calculated, and if this ratio is large (~ 7), then it may be assumed that the C—H bond is broken in the slow-step of the reaction.

Deuterium and hydrogen are chemically similar, but the former is heavier (it has one proton and one neutron in its nucleus). For this simple reason, deuterium vibrates (moves towards and away from the nuclei to which it is bonded) slower than hydrogen. As a result the C—H bond is more easily broken than the C—D bond and therefore, so is the rate of a reaction in which a C—H bond cleavage is the slow step. In other words, although in the ground state of the reactant, the C—D bond possesses a greater stability than the corresponding C—H bond. There is, however, no difference in the energy in the transition state as both are equally stretched. The difference lies in the activation energy needed to break the C—D and C—H bonds which is larger for the former. Since the activation energy of a reaction is related to the rate constant, the K_H/K_D rate ratio will be greater than one, i.e. $K_H/K_D > 1$. The maximum kinetic isotope effect for a reaction has been observed to be 7 at room temperature. If the K_H/K_D rate ratio is equal to unity then there is no isotope effect and it can be concluded that a C—H bond is not broken in the rate-determining step of that reaction.

QUESTIONS

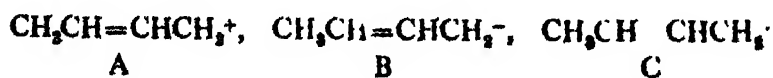
5.1 Write short notes on the following:

Activated complex, a first order reaction, intermediate, activation energy, rate-controlling step, chemical equilibrium, stereospecific *cis*-addition and the mechanism of ester hydrolysis.

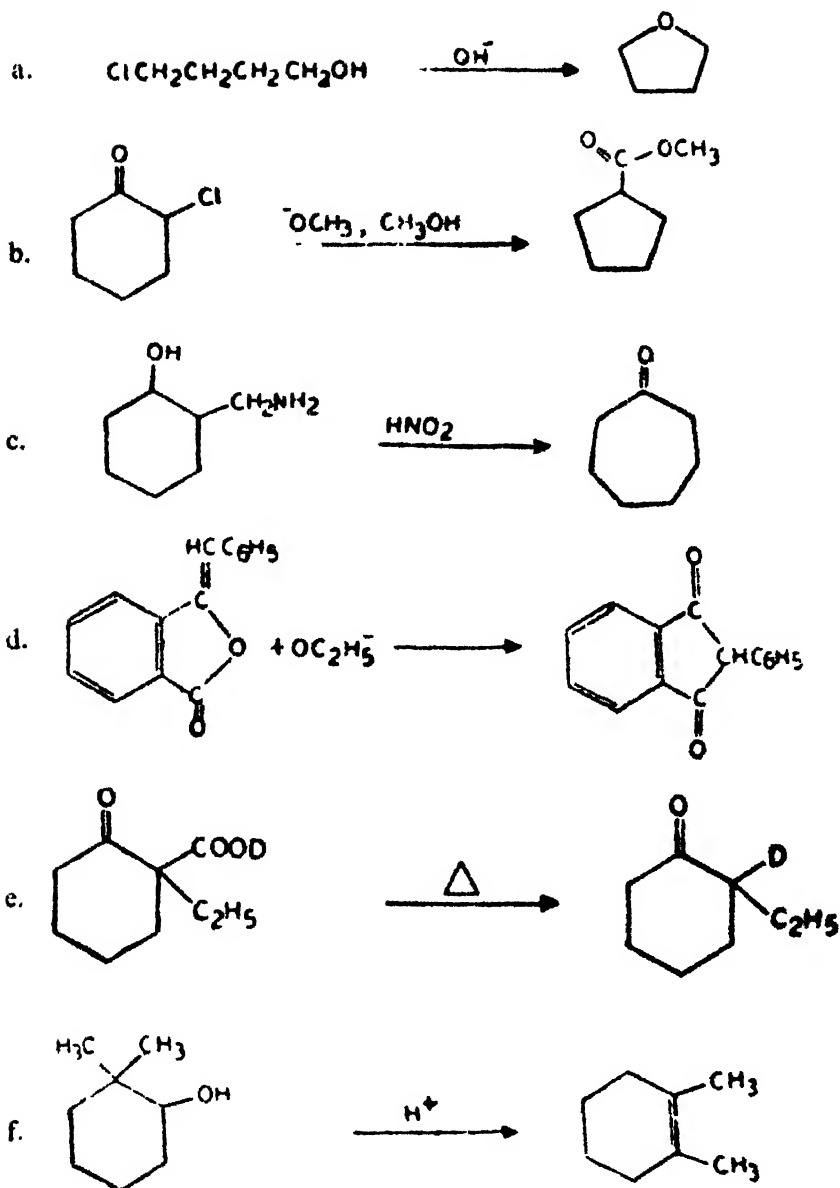
5.2 Describe, with appropriate examples, stereochemical studies as a probe for investigating reaction mechanisms.

5.3 Account for the following:

The species A, B and C are more stable than D, E and F respectively.

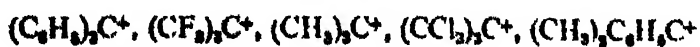


5.4 Suggest a plausible mechanism for each of the following reactions:

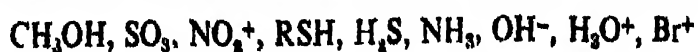


5.5 The bromination of acetone in the presence of Br_2 and HBr ,
 $\text{CH}_3\text{COOCH}_3 + \text{Br}_2 \xrightarrow{\text{HBr}} \text{CH}_3\text{COCH}_2\text{Br} + \text{HBr}$ has the rate law,
 rate $\sim k [\text{CH}_3\text{COCH}_3] [\text{H}^+]$. Suggest a mechanism for this reaction.

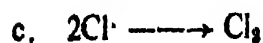
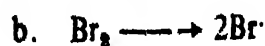
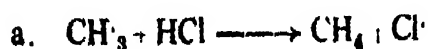
5.6 Write in the increasing order of stability:



5.7 Separate the following species into electrophiles and nucleophiles:



5.8 Sketch potential energy diagrams for the following reactions and label E_a and ΔH :



★ Purification and Structure Determination of Organic Compounds

Organic compounds are either synthesized in the laboratory or isolated from natural sources. The compounds obtained from natural sources are alkaloids, terpenes, proteins, etc. One of the principal aims of an organic chemist is the purification and structure establishment of unknown compounds. Several methods are available to achieve purification of a sample, whether it is solid or liquid. The purified compound is subjected to elemental analysis to ascertain the nature and the proportion of the elements present. Based on the types and number of elements, the functional group is established. Determination of molecular weight and the molecular formula is the next logical step. From the data, one can arrive at some reasonable structure of the compound, at least in certain simple cases. The postulated structure can be confirmed by carrying out some appropriate chemical reactions. A final proof is, of course, obtained by using modern spectroscopic techniques such as ir, uv, nmr, etc. discussed at the end of the chapter.

Separation

6.1 METHODS FOR THE PURIFICATION OF SOLIDS

The product obtained from a chemical reaction is often crude and contaminated with impurities. As a result, the melting or boiling point of the compound is not sharp. The compound needs to be purified, and, in the case of a solid any one of the following methods may be used.

6.1.1 Recrystallization

In this method the impure substance is dissolved in a suitable solvent (at its boiling point), and then allowed to cool at room temperature. During cooling, the pure substance crystallizes out from the solution whereas the impurities remain dissolved in the solvent. To obtain purification according to this method, a proper solvent must be found because the process depends on the differential solubility of a substance in the hot and a cold solvent. It is highly desirable that the substance should have a high solubility in the hot solvent

but low solubility in the cold solvent. Sometimes a mixture of two solvents may have to be used. Samples often contain some colored impurities which can be removed during recrystallization. To do this, a small amount of decolorizing carbon or *Norit* is added to the solution of the substance, and the solution is refluxed for 15 min and then filtered hot. In a recrystallization, the crystals from a hot solution should commence to appear as soon as the solution is allowed to cool. However, if this does not happen, one may have to resort to some other means. This may include cooling the solution in an ice-bath; scratching the sides of the container with a glass rod or adding a crystal of the compound. This last method is called *seeding*. If all attempts fail, then probably there is too much solvent, so part of it is removed by boiling. In general, two or more recrystallizations may be needed to obtain a satisfactory purification.

6.1.2 Fractional Crystallization

This is a useful method for the separation of a mixture of two compounds which differ only slightly in solubility. A typical example is the separation of enantiomers of an optically active compound. The process resembles recrystallization in that the solution of the mixture is allowed to cool at room temperature, whereby one of the components recrystallizes out preferentially in a large proportion. The mother liquor is concentrated until crystallization occurs. The crystals are removed again and components of reasonable purity are obtained. This method has its own drawback as it is time consuming. The process can, however, be speeded up if pure crystals, preferably of the less soluble compound are available by a process known as *seeding*.

6.1.3 Sublimation

This is a useful method for the purification of those substances which have sufficiently high vapor pressure and pass directly from the solid to the vapor phase. The vapor pressure of such substances reaches 760 mm, the atmospheric pressure, before the melting point is reached. The substance then on heating at 1 atm, will pass directly to the vapor phase at its sublimation temperature. The substance is often heated under reduced pressure. The vapors come in contact with a cold surface and solidify. This method is used in the commercial purification of several organic chemicals; some examples are: carbon dioxide (mp 57°, v.p. 5.2 atm) hexachloroethane (mp 186, v.p. 0.780 mm), naphthalene (mp 80, v.p. 7 mm), camphor (mp 179, v.p. 370 mm), etc.

6.2 METHODS FOR THE PURIFICATION OF LIQUIDS

Entirely different methods such as distillation, counter-current extraction, or fractional freezing are available for the separation and purification of liquids. Among these, distillation is the most common method of purification.

Chromatographic techniques, to be discussed in the next section, are also applied both for liquids and solids. *Distillation* may be described as the partial vaporization of a liquid, the carrying over and the condensation of these vapors in a different part of the distillation apparatus. Various types of distillation techniques are used by an organic chemist, such as simple distillation, fractional distillation and steam distillation.

6.3 CHROMATOGRAPHIC METHODS

A widely used technique for the separation of a desired compound from its impurities or a mixture of compounds into its components is chromatography. The name to this technique was given by the Russian chemist, Tswett at the turn of the century. He used it for the separation of colored compounds (*Chroma*, color). Analogous to extraction, chromatography also depends on the principle of phase distribution. In this technique the components of a mixture are selectively adsorbed on a stationary phase and are then dislodged from it by a second mobile phase.

Various types of chromatographic methods are classified according to the physical states of the different phases involved, i.e. stationary and mobile. The mobile phase can be gas or liquid, while the stationary phase can be solid or liquid. When the separation involves partitioning between two liquid phases (one of them adsorbed on the solid phase) then it is referred to as *partition chromatography* or *liquid-liquid chromatography*. Those in which solid-liquid interactions take place are classified as *Column Chromatography*, *high pressure liquid chromatography* and *ion exchange*. In *gas chromatography* (glc), on the other hand, the mobile phase is a gas while the stationary phase is a liquid coated on a solid.

Gel chromatography or *gel filtration* is a case of an exclusion chromatography in which the solid phase is a gel and separation takes place on the basis of molecular sizes.

6.3.1 Column Chromatography

In this type of chromatography the separation is effected by adsorption on a solid phase. Several types of interactions that cause interactions of the molecules with the solid are hydrogen bonding, van der Waals forces, electrostatic interactions. A cylindrical glass column of the type shown in Fig. 6.1 is employed to separate a mixture by column chromatography.

To pack a column, first clean it thoroughly and dry. Now position it vertically on an iron stand with the help of a clamp. Close the stopcock and fill the column with an appropriate solvent. Insert a small plug of glass wool with a rod to the bottom. Pour some dry sand so that it forms a 1-cm layer on the top of the glass wool. Add slowly alumina or a slurry (it is silica) on the top of the column with constant tapping the sides of the column. Open the stopcock and allow the solvent to drain out simultaneously at a rate of 1-2 drops per sec. When all the adsorbent has been added, introduce more sand to form a 1-cm layer at the top of the silica layer.

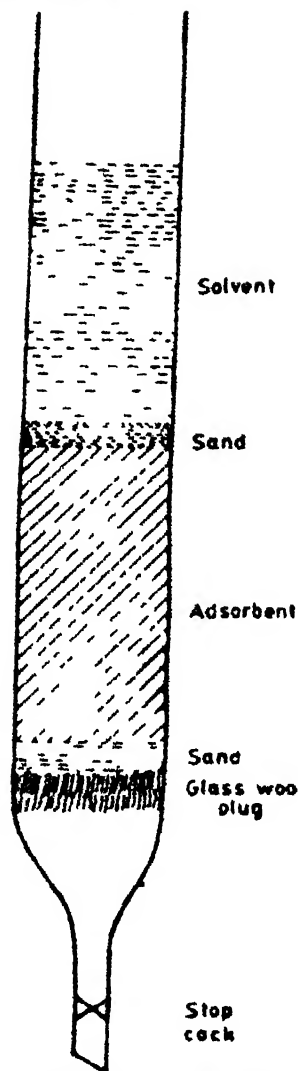


Fig. 61 A Packed Chromatographic Column

The column is now ready for use. The adsorbents of common choice are alumina, silica gel, cellulose, charcoal, etc. Several considerations govern the choice of an adsorbent. It should be insoluble in the solvent and must not react with the substance to be separated. The sample is then taken in a minimum amount of a solvent and introduced from the top of the column. Then a suitable solvent (mobile phase) is allowed to percolate through the column. The process is known as *elution*. It is customary to use a relatively non-polar solvent in the beginning. The adsorption depends on both the nature of the solvent and the adsorbent. For effective separation the eluting solvent must be significantly less polar than the components of the mixture. In case the solvent is more polar and strongly adsorbed than the components of the mixture, the components will remain in the mobile phase and

little, if any, separation will take place. It is also essential that the mixture is soluble in the solvent, otherwise it will remain permanently adsorbed on the adsorbent. Polar solvents are used for eluting strongly adsorbed components while non-polar solvents are used for weakly adsorbed components of a mixture. An approximate order of increasing polarity of some common solvents is as follows: petroleum ether, hexane, carbon tetrachloride, toluene, chloroform, and water. A mixture of two solvents may be more useful for separation in many instances.

6.3.2 Thin Layer Chromatography (TLC)

Thin layer chromatography involves the same principle as column chromatography. It is a form of solid-liquid adsorption chromatography in which the stationary phase is spread on a glass plate. Izmarlov and Shraiber in 1938 developed this technique. However, it was due to the efforts of Stahl (1958) that his technique was ultimately accepted as a new modern technique of analytical chemistry. This method is simple, rapid in separation

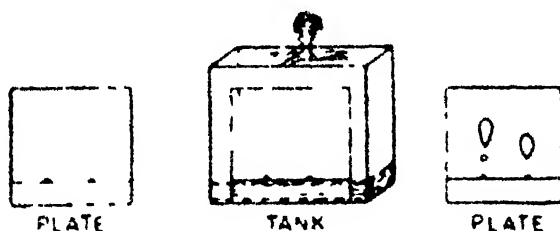


Fig. 6.2 A TLC Plate and Tank

and very efficient. There are different ways of coating the glass plates with the adsorbent such as pouring, dipping, spraying and spreading. The solid adsorbent is spread in a thin layer (0.25 mm thickness) on a glass plate with the help of a spreader. Among the adsorbents used, silica and alumina are most common. It is also more finer and is mixed with a small amount of "binder", so that the adsorbent does not flake off on drying the plate. The sample is applied as a solution in a non polar solvent at one end of the plate in the form of a symmetrical spot (use a syringe or a capillary tube). It is often necessary to repeat this process in order to get several milligrams of the sample on the plate. The plate is dried and then placed in a chamber saturated with the solvent. Solvent for development is selected on the basis of the nature of the components. The various components are then separated depending on the preferential adsorption on the plate. After the solvent has moved a distance of approximately 10 cm on the plate, it is taken out of the chamber and dried. The detection of spots on the chromatogram is easy for colored compounds. The colorless compounds can be visualized by a number of reagents. For ins-

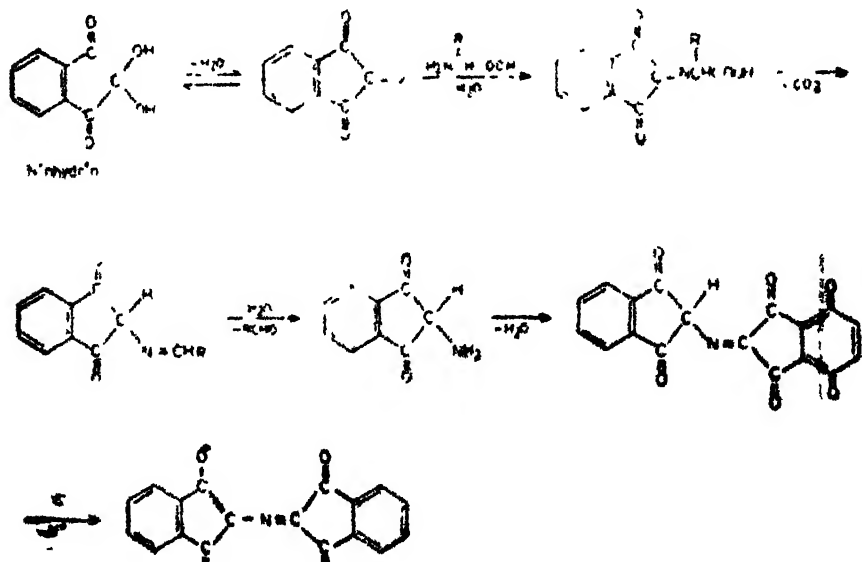
tance, sulfuric acid, KMnO_4 solution or *p*-anisaldehyde can be sprayed on the plate and the spots are revealed as colored compounds. Iodine is another reagent which is widely used. In this case, the plate is placed in a closed container containing some iodine crystals. The iodine vapors are adsorbed into the areas of the plate containing the organic compound and brown spots due to the formation of iodine charge-transfer complexes appear. Sometimes exposure of the plate to uv light permits location of the spots for compounds that fluoresce.

Under a given set of conditions (adsorbent, solvent, thickness, etc.) TLC can be used for identification purposes also. For this purpose R_F value which is the ratio of the distance travelled by the substance from the origin to the distance travelled by the solvent from the origin is measured

$$R_F = \frac{\text{Distance travelled by the substance}}{\text{Distance travelled by the solvent front}}$$

6.3.3 Paper Chromatography ✓

Paper chromatography is similar to thin layer chromatography. In this technique a small spot of the sample is placed near one end of a strip of filter paper. The paper strip is suspended in a jar in such a way that the end of the paper strip is immersed in the developing solvent. In this case a distribution takes place between water (adsorbed by the filter paper to an extent of 20%) and the mobile solvent. It is for this reason it is also referred to as liquid-liquid partition chromatography. The different compounds may be identified by calculating the R_F values. Paper chromatography is useful for polar molecules like amino acids. The individual samples of amino acids are visualized by spraying with ninhydrin solution (0.1% solution in 95% ethanol) and blue-violet colors are produced. The color forming reaction takes place as follows:



Most of the amino acids give blue color (except proline which gives a yellow color) it indicates that the colored product formed is the same

6.3.4 Ion-Exchange Chromatography

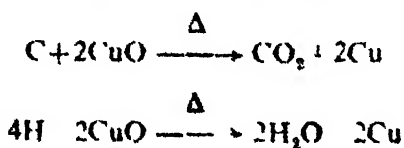
Ion-exchange resins are polymeric substances that contain polar groups and are capable of exchanging their groups with the ion of the solution of an electrolyte. Nowadays a large range of ion-exchange resins have been developed. These are usually prepared by copolymerization of styrene and divinylbenzene which results in a highly cross-linked three-dimensional network. This is then subjected to substitution reactions resulting in the introduction of functional groups. These functional groups can be strong acids (sulfonic acid, carboxylic acids and phenols) or strong bases (quaternary ammonium hydroxides). Ion exchange resins are often classified as cation or anion-exchange resins depending on whether a cation (H^+ , Na^+ , NH_4^+ , etc.) from acidic groups or their salts, or an anion (Cl^- , OH^- , etc.) from a quaternary salt group is exchanged. This technique is used similar to column chromatography.

6.4 ESTIMATION OF ELEMENTS

The quantitative analysis of an organic compound is essentially the most important step in structure determination. We will describe briefly the principles of several methods, without going into the experimental details.

6.4.1 Carbon and Hydrogen

These two elements are estimated by the method of *Liebig and Gay-Lussac*. In this method, an organic compound is subjected to combustion at 700–800°C in the presence of copper oxide. The products of combustion, namely carbon dioxide and water, are swept along with a stream of dry nitrogen and absorbed in tubes containing potassium hydroxide and calcium hydroxide respectively. From the amounts of CO_2 and H_2O absorbed, the percentages of carbon and hydrogen are calculated.



Weight of substance taken	w g
Weight of carbon dioxide formed	w_1 g
Weight of water formed	w_2 g
Weight of carbon in the sample	$= 12/44 \times w_1$
% Carbon in the sample	$12/44 \times w_1 / 100 \times w$
Weight of hydrogen in the sample	$2/18 \times w_2$
% Hydrogen in the sample	$2/18 \times w_2 / 100 \times w$

The amount of oxygen is difficult to determine directly, it is often calculated by difference.

6.4.2 Nitrogen

Nitrogen, in an organic compound, may be estimated by either of the following two familiar methods.

(a) *Dumas Method*: A weighed amount of the nitrogenous compound is mixed with cupric oxide and the mixture is heated in an atmosphere of carbon dioxide. Nitrogen gas is produced, which is collected in a nitrometer and its volume measured. The corresponding temperature and pressure are also noted. It is also necessary to know the vapor pressure of water under these conditions, which should be subtracted from the measured pressure, to determine the pressure due to nitrogen only.

Weight of the sample w g

Volume of nitrogen evolved $= V$ ml

We know that 22.4 lit of any gas weighs equal to its molecular weight at normal temperature and pressure. Convert the volume V of nitrogen to N.T.P. and assume it is equal to V_1 . For nitrogen 22,400 ml of N_2 = 28 g, and

$$V_1 \text{ ml of nitrogen} = \frac{28 \times V_1}{22,400} \text{ g}$$

This is equivalent to the weight of nitrogen in the sample

$$\therefore \% \text{ Nitrogen} = \frac{28 \times V_1}{22,400} \times 100$$

(b) *Kjeldahl's Method* The estimation of nitrogen is frequently carried out in the laboratory by this method. The sample is digested with measured quantity of conc. sulfuric acid and a catalyst [a mixture of potassium sulfate (20g), selenium powder (1g) and cupric sulfate, $CuSO_4 \cdot 5H_2O$, (2g)]. During digestion, the compound is converted into ammonium sulfate. Then, an excess amount of sodium hydroxide solution is added and ammonia gas is steam distilled and absorbed in excess standard sulfuric acid solution. The remaining acid is back-titrated against standard sodium hydroxide solution. The percentage of nitrogen is calculated as follows:

Weight of nitrogen containing compound w g

Volume of 0.1 N H_2SO_4 taken = 50 ml

Volume of 0.1 N NaOH required to back titrate excess H_2SO_4 = V ml

Volume of 0.1 N H_2SO_4 used for reaction with the evolved ammonia
 $= (50 - V) \text{ ml}$

(50 - V) ml of 0.1 N H_2SO_4 = (50 - V) ml of 0.1 N NH_3

1000 ml of 1 N NH_3 = 17 g of NH_3 or 14 g of nitrogen

1000 ml of 0.1 N NH_3 corresponds to 1.4 g of nitrogen

(50 - V) ml of 0.1 N NH_3 corresponds to $\frac{(50 - V) \cdot 1.4}{1000}$ g of nitrogen

$$\% \text{ Nitrogen} = \frac{(50 - V) \times 1.4}{1000} \times \frac{100}{w}$$

6.4.3 Halogens

Halogens (Cl_2 , Br_2 , I_2) are estimated by the *Carius method*. A weighed amount of the substance is heated with fuming nitric acid and silver nitrate solution in a sealed tube, known as the Carius tube. The halogen is converted to the corresponding silver halide which is washed dried and weighed. The percentage of halogen is calculated as follows:

Weight of the sample = w g

Weight of silver chloride formed = W g

143.5 g (108 + 35.5) of $AgCl$ contains 35.5 g of Chlorine

W g of $AgCl$ contains $\frac{35.5}{143.5} \times W$ of chlorine

$$\% \text{ Chlorine} = \frac{35.5}{143.5} \times \frac{W}{w} \times \frac{100}{w}$$

$$\text{similarly } \% \text{ Bromine} = \frac{80}{188} \times \frac{W_1}{w} \times \frac{100}{w}$$

where W_1 is the weight of $AgBr$.

6.5 DETERMINATION OF MOLECULAR WEIGHT

The molecular weight of a substance is defined as the number of times its molecule is heavier than that of a hydrogen atom. Depending on the nature of the compound, the following two methods are employed for its determination.

6.5.1 Victor Meyer's Method

This method is employed for volatile liquids. A known quantity of the liquid is volatilized in a Victor Meyer tube. The volume of the vapors evolved is measured and then reduced to N.T.P. using Boyle's law.

Weight of the liquid = w g

Volume of vapor at N.T.P. = V ml

V ml of the liquid corresponds to w g

$$22,400 \text{ ml corresponds to } \frac{22,400 \times w}{V} \text{ g}$$

which is the molecular weight of the liquid.

6.5.2 Depression of Freezing Point

This method is useful for non-volatile solids. A known weight of the compound is dissolved in a known quantity of a suitable solvent of known melting point (such as camphor) and the melting point of the mixture is determined. The difference in the two melting points yields the depression in the freezing point. The molecular weight (m) is given by the following expression :

$$m = \frac{100 \times K_f \times w}{W \times \Delta T}$$

where K_f is the molal depression constant

w — weight of the compound

W — weight of the solvent

ΔT — depression in freezing point

6.6 DETERMINATION OF EQUIVALENT WEIGHT OF AN ACID AND BASE

Volumetric or gravimetric methods may be employed to determine the equivalent weight of an acid and base.

6.6.1 Volumetric Method

This method is applicable both for acids and bases. A weighed amount of an acid or base is dissolved in water (or aqueous ethanol or dioxane) and then titrated against a standard solution of a base or acid solution, as the case may be. The molecular weight can be calculated from the equivalent weight

Weight of the acid = w g

Suppose l ml of 0.1 N NaOH is needed to neutralize w g of the acid

1000 ml of 0.1 N NaOH will require $\frac{1000}{l} \times 0.1 \times w$ g

1000 ml of 1 N NaOH will require $\frac{1000}{1} \times 0.1 \times w \times \text{N}$ g

where N is equal to unity

This is the equivalent weight of the acid, the molecular weight is obtained by multiplying it with its basicity which is equal to the number of hydrogen atoms which will react with a base. The molecular weight of the base is evaluated similarly

6.6.2 Silver Salt Method (For Acids)

The ammonium salt of a carboxylic acid is converted to its silver salt using silver nitrate solution. The silver salt of the acid is ignited which leaves a residue of metallic silver while the carbonaceous materials are volatilized.



Weight of silver salt = w g

Weight of metallic silver = w_1 g

Equivalent weight of the silver salt = $\frac{\text{Weight of silver salt}}{\text{Equivalent weight of silver}}$

Equivalent weight of silver salt = $\frac{w}{\frac{w_1}{108}}$ 108

Equivalent weight of the acid = $\left(\frac{w}{\frac{w_1}{108}} - 108 \right)$ 107

Molecular weight of the acid = $\left[\left(\frac{w}{\frac{w_1}{108}} - 108 \right) \times \text{basicity} \right]$

6.6.3 Chloroplatinic Salt Method (For Bases)

This method is based on the fact that organic bases, for instance amines, react with chloroplatinic acid (H_2PtCl_6) to form water soluble chloroplatinates of the general formula $\text{B}_2\text{H}_2\text{PtCl}_6$. These salts easily decompose on heating to yield metallic platinum.

Weight of the platinum salt taken = w g

Weight of platinum obtained = w_1 g

Molecular weight of the salt = $2B + 410$

where B represents the equivalent weight of the base.

Weight of platinum = $\frac{\text{Atomic weight of platinum (195)}}{\text{Molecular weight of salt}}$

Molecular weight of salt = $\frac{195 \times w}{w_1}$

$2B + 410 = \frac{195 \times w}{w_1}$

$B = \frac{1}{2} \left(\frac{195 \times w}{w_1} - 410 \right)$

Since B represents the equivalent weight of the base, its molecular weight is obtained by multiplying it with its acidity.

6.7 CALCULATION OF EMPIRICAL AND MOLECULAR FORMULA

The *empirical formula* of a compound is described as the simplest formula which gives the ratio in whole numbers, in which the different elements are present. *Molecular formula* represents the actual number of different atoms present in the molecule. These two have the following relationship:

Molecular formula - (Empirical formula)_n

where $n = \frac{\text{Molecular weight}}{\text{Empirical formula weight}}$

This can be illustrated by the following examples.

6.7.1 An organic compound on analysis gives C - 41.35%; H - 6.89% and N = 24.12%. Determine its empirical formula

Element	Percentage composition	Atomic weight	Relative number of atoms		Simplest ratio	
C	41.35	12	$\frac{41.35}{12}$	3.44	$\frac{3.44}{1.72}$	2
H	6.89	1	$\frac{6.89}{1}$	6.89	$\frac{6.89}{1.72}$	4
N	24.12	14	$\frac{24.12}{14}$	1.72	$\frac{1.72}{1.72}$	1
O	27.64	16	$\frac{27.64}{16}$	1.72	$\frac{1.72}{1.72}$	1

The percentage of oxygen was obtained by difference.

The empirical formula is C_2H_4NO

6.7.2 An organic compound contains C - 52.17%, H - 13.05%, O - 34.48%. Its vapor density is 22.9. Calculate its molecular formula.

Element	Percentage composition	Atomic weight	Relative number of atoms		Simplest ratio	
C	52.17	12	$\frac{52.17}{12}$	4.34	$\frac{4.34}{2.15}$	2
H	13.05	1	$\frac{13.05}{1}$	13.05	$\frac{13.05}{2.15}$	6
O	34.48	16	$\frac{34.48}{16}$	2.15	$\frac{2.15}{2.15}$	1

Empirical Formula is C_2H_6O

Empirical formula weight = 46

Molecular weight of the compound = $2 \times \text{vapor density}$

$$2 \times 22.9$$

$$= 45.8$$

$$n = \frac{45.8}{46} = 1$$

Molecular formula $(C_2H_6O)_1$

Since $n = 1$, therefore the molecular formula is also C_2H_6O

6.7.3 A 0.234 g of organic compound containing nitrogen was Kjeldahlized and the ammonia gas evolved was absorbed in 90.35 ml of 0.1 N HCl. The unused acid required 20.00 ml of 0.2N NaOH for complete neutralization. Calculate the percentage of nitrogen in the sample.

Assume the volume of HCl unused = x ml

$$x \times 0.1 = 20.00 \times 0.2$$

$$\text{or } x = 40.00$$

Volume of acid used = $90.35 - 40.00 = 50.35$

Using the relationship in Sec. 6.4.2b

$$\%N = \frac{14}{1000} \times 50.35 \times 0.1 \times \frac{100}{0.234} = 30.12$$

6.7.4 An organic acid, on analysis gave the following result : 0.1 g of the acid on combustion yielded 0.252 g of CO_2 and 0.0444 g of H_2O . A 0.122 g sample of the acid required 10 ml of 0.1 N alkali for complete neutralization. Calculate the molecular formula.

$$C = \frac{12}{44} \times 252 \times \frac{100}{0.1} = 68.73$$

$$H = \frac{2}{18} \times 0.044 \times \frac{100}{0.1} = 4.88$$

$$O \text{ (By difference)} = 26.39$$

Empirical Formula obtained is C_7H_6O ; Empirical formula weight = 122
10 ml of 0.1 N alkali neutralizes 0.122 g of the acid

$$1 \text{ ml of } 1 \text{ N } \therefore \quad \therefore \quad \frac{0.122}{10} = 10$$

$$1000 \therefore \quad 1 \text{ N } \therefore \quad \therefore \quad 0.122 \times 10 \times 1000 = 122$$

$$\therefore n = \frac{122}{122} = 1$$

Therefore, the molecular formula $C_7H_6O_2$

6.7.5 A monoacid organic base on analysis yielded the following results : 0.1 g of the base gave 0.28 g of CO_2 , and 0.075 g of water and, 0.2 g of the base gave 21.8 ml of nitrogen measured at $15^\circ C$ and 760 mm, 0.30 g of the platinum chloride left on ignition 0.093 g of platinum. What is the molecular formula of the base?

$$\%C = 12.44 \times 0.28 \times 100/0.1 = 76.36$$

$$\%H = 2/18 \times 0.075 \times 100/0.1 = 8.33$$

$$\%N = \frac{28 \times 21.8 \times 100}{24000 \times 0.3} = 13.05$$

[22,400 ml is volume of one mole of nitrogen at N.T.P.]

Empirical formula obtained is C_7H_9N . Using the relationship on p. 117, the molecular weight of the base is given by:

$$B = \frac{1}{2} \left[\frac{195 \times 0.3}{0.093} - 410 \right] = \frac{1}{2} [629 - 410]$$

$$B = 109.5$$

$$n = 109.5/107 = 1$$

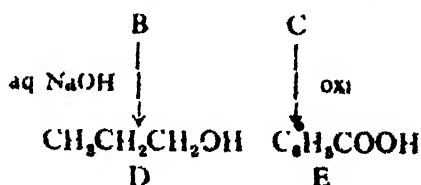
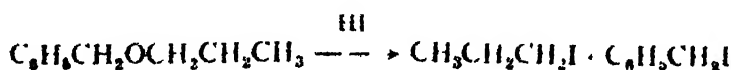
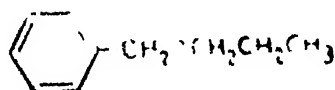
Molecular formula C_7H_9N

6.8 SOLVED EXAMPLES

The previous section was concerned with the determination of the molecular formula of the compound. The elucidation of the actual structure of the compound could become complicated, but could be solved by a sound knowledge of chemical reactions. Several representative examples will be worked out here to make the student familiar with the procedure.

6.8.1 Compound A, $C_{10}H_{14}O$ does not react with bromine, acetyl chloride or boiling aqueous sodium hydroxide solution. Boiling hydriodic acid, however, converts A into two compounds B, C_8H_8I and C, C_7H_7I . B, can be hydrolyzed by aqueous sodium hydroxide to D, C_8H_7OH , which does not give a positive Lucas test. C, can be oxidized to a carboxylic acid, E, $C_6H_5CO_2H$ by chromic acid. Assign structures to the lettered compounds.

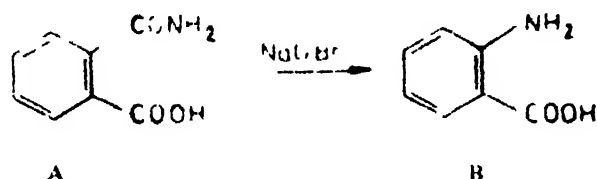
Since the compound does not react with any of the reagents, it is not a phenolic derivative. The reaction with HI also excludes an aldehyde or ketone. It is probably an aromatic ether with the following structure:



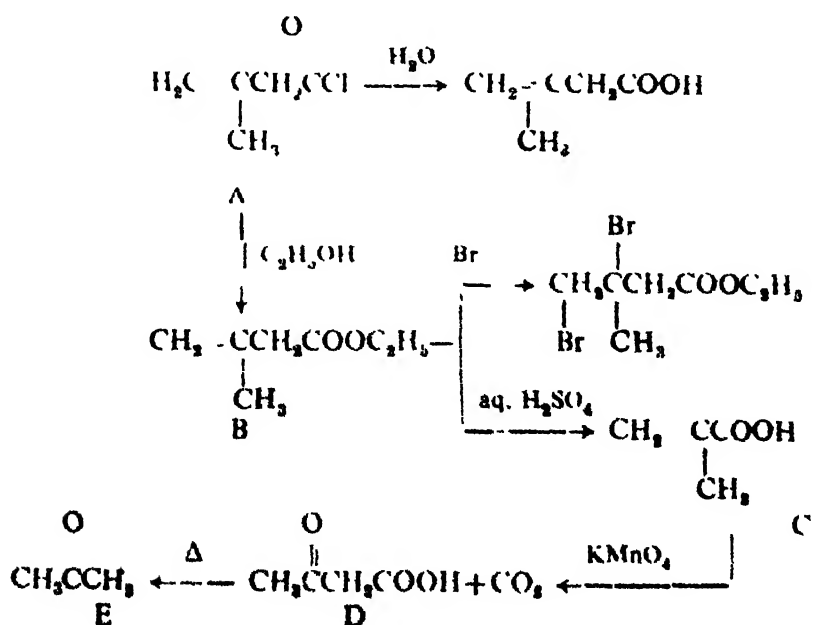
D, is a primary alcohol because it does not respond to Lucas reagent

6.8.2 An organic compound A, contains C - 58.2%, H - 4.2% and N - 8.2%. On heating with sodium hydroxide, it evolves ammonia but does not undergo diazotization or react with acetyl chloride. On reaction with sodium hydrobromite, A yields an acid B, $C_7H_7O_2N$, which dissolves both in base and in acid. What are compounds A and B?

The empirical formula can be calculated to be $C_8H_9NO_2$. Since A cannot be diazotized or undergo reaction with acetyl chloride, it does not contain a primary amino group or a hydroxyl group. It responds to the Hofmann bromamide reaction, therefore, it contains an amide group. Thus, A and B have the following structures

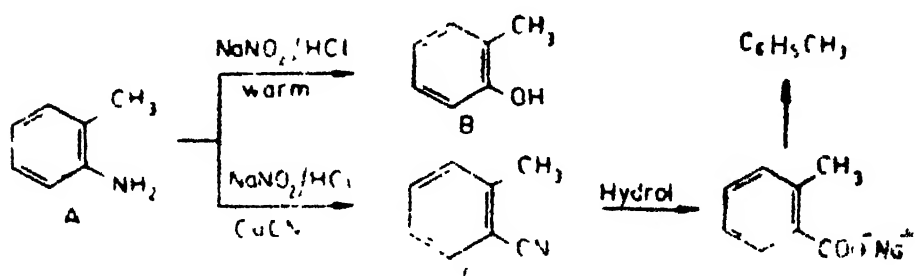


6.8.3 Compound A, C_6H_7OCl , reacts rapidly with ethanol to form a pleasant-smelling substance, B, $C_7H_{12}O_2$. A, also reacts rapidly with water to produce an acidic substance, B. Bromine water reacts with B, to yield $C_7H_{11}O_4Br_2$. B, on boiling with aqueous sulfuric acid, forms an acid C, with a neutralization equivalent equal to 100 ± 1 . When C is oxidized vigorously with permanganate solution a new acid D, $C_4H_6O_3$, and CO_2 result. Carbon dioxide is evolved on mild heating of D, along with E, C_3H_6O which is not oxidized by Tollens reagent.



6.8.4 Compound A, C_7H_9N , is insoluble in water but dissolves rapidly in dil hydrochloric acid. When $NaNO_2$ is added to the solution and the mixture warmed, a gas is evolved to produce a product B, C_7H_9O which is insoluble in sodium hydroxide solution. On the other hand, if $NaNO_2$ is added to an ice cold solution of A in HCl, and the resulting solution is treated with cuprous cyanide, a compound C, C_8H_7N , is formed. Alkaline hydrolysis of C yields a sodium salt of an acid which on fusion with soda lime yields toluene. Write the structures of A, B and C.

The first reaction suggests that it is an aromatic amine and all the other reactions can be explained as follows.



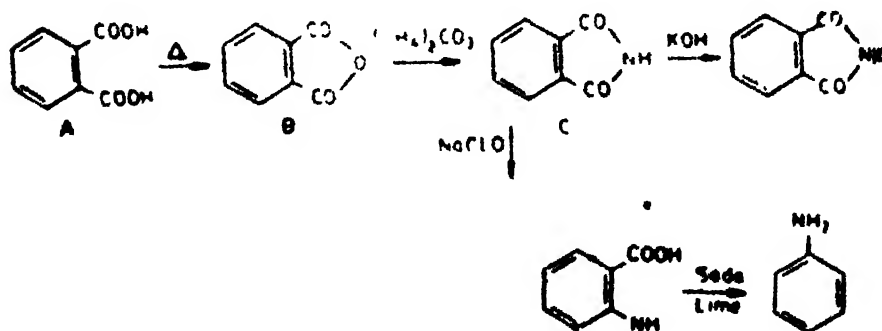
6.8.5 An Organic dibasic acid A, yielded on analysis C = 57.8%, H = 3.6%. Its silver salt contained 56.8% silver. On heating it forms a compound B, $C_8H_4O_3$, which reacts with $(NH_4)_2CO_3$ to form another compound C, $C_8H_5O_2N$. Compound C forms a potassium salt with alcoholic KOH and a compound D, on treatment with alkaline $NaClO$. Compound D, on dry distillation with soda lime forms aniline. Give the structures of A, B, C and D.

The empirical formula of A is $C_8H_5O_4$, using the relationship on p. 117, the molecular weight of the acid

$$\left(\frac{100}{56.8} - \frac{109}{2} \right) \cdot 2 = 166$$

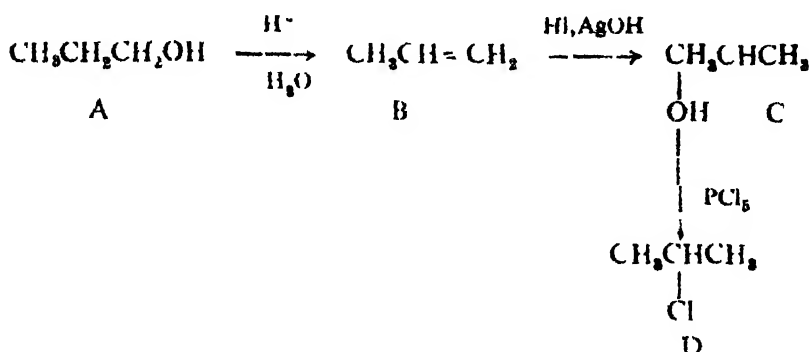
$$n = \frac{166}{83} = 2$$

Molecular formula $C_8H_5O_4$



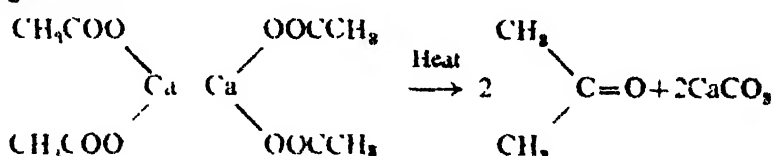
6.8.6 An alcohol, A (vapor density 30) gave on dehydration a hydrocarbon, B, containing C, 85.7%, and H, 14.3%. B, on successive reactions with hydrogen iodide and moist silver oxide gave, C, which is isomeric with A. When C was treated with phosphorus pentachloride, D was obtained which contained Cl, 45.2%. Explain these reactions and assign structures to A, B, C and D.

Since alcohol A has a molecular weight of 60, its molecular formula would correspond to $C_3H_7.OH(C_nH_{2n+1}.OH)$. On dehydration, an unsaturated hydrocarbon is obtained which contains C, 85.7%, and H, 14.3%, therefore, the structures are

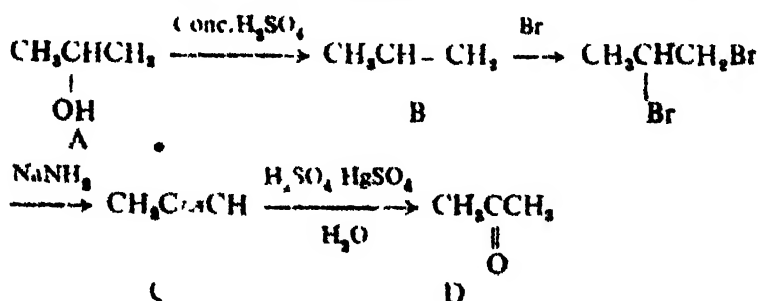


6.8.7 An alcohol A, on treatment with conc. sulfuric acid gives an alkene B. The compound B, on bubbling through bromine-water and subsequent dehydrogenation with excess sodamide yields a new compound C. When C is treated with warm dilute sulfuric acid in the presence of HgSO_4 it gives D. This compound (D) can also be obtained either by oxidizing A with KMnO_4 or from acetic acid through its calcium salt. Identify A, B, C and D.

Since calcium salt yields compound D, it is acetone, according to the following reaction



Compound D is alternatively obtained by oxidizing A, therefore, A is 2-propanol. The following reaction sequence thus identifies the compounds



6.9 SPECTROSCOPIC METHODS

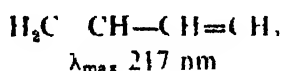
To ascertain the structure of an unknown organic compound, whether obtained by a synthetic process or from a natural source, is a fundamental operation in chemistry. Different physical constants such as m.p., refractive index, etc. can be determined, but such data may be employed only for characterization and elementary identification of an organic compound. A direct elucidation of the structure after preliminary investigations have been made, involves a consideration of its physical properties. The most useful physical property for this purpose is spectra. Spectroscopy has become a useful tool for structure determination. It may be described as a technique whereby we measure the amount of radiation absorbed by a substance at various wavelengths, from the spectra useful information about the structure of the compound can be obtained. Different types of spectroscopic techniques are available nowadays. Though the mechanism of absorption energy differs in the i.r. and n.m.r. regions the fundamental process involves the absorption of certain amount of energy. The energy (E) absorbed by a molecule is related to the frequency of electromagnetic radiation and is given by $E = h\nu$ where h is the Planck's constant (6.624×10^{-27} erg sec) and ν is the frequency (in cycles/sec., cps) of radiation. The frequency is related to wavelength by the expression $\nu = c/\lambda$ where c is the velocity of light (2.998×10^{10} cm/sec) (and λ is wave length in cm). There are many forms of radiant energy and a wide range of high energy rays at one end to radio waves at the other end constitutes the electromagnetic spectrum. The regions that interest an organic chemist are the ultraviolet (2000-4000 Å), the visible (4000-8000 Å) and the infrared (2.5-15 μ), where $1 \mu = 10^{-4}$ cm. The spectroscopic methods, as will be seen in this section, possess many advantage over the chemical methods of analysis. Spectroscopic methods require much less time, require only a small amount of the sample which in many cases remains unchanged during analysis and, above all, these methods are more reliable.

In this section an introductory account of the spectroscopic techniques, namely uv, ir, and nmr will be given. The purpose is to make the student aware of the immense utility of these methods for structure determination.

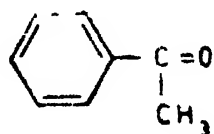
6.9.1 Ultraviolet Spectroscopy

The absorption of radiation in the ultraviolet and visible region of the spectrum depends on electronic structure of the molecule. Absorption of energy by a molecule results in the excitation of electrons from low-energy orbitals in the ground state to the high-energy orbitals. All molecules, however, do not absorb energy in the readily accessible portion of the uv region. As a consequence uv spectrometry for the most part is limited to conjugated systems which absorb at more convenient wavelengths. The ultraviolet region of the electromagnetic spectrum extends over the wavelength range of 2000-4000 Å ($1 \text{ Å} = 10^{-8}$ cm) or 200-400 nm ($1 \text{ nm} = 10^{-7}$ cm). The magnitude of the energy required for electronic transitions is of the magnitude of bond strengths, i.e. 70-300 Kcal/mole.

The absorption of energy by organic molecules in the uv or the visible region involves the excitation of electrons in σ , π and n orbitals from the ground state of the higher-energy states. Thus, the absorption of light from a π -bonding to a π -anti-bonding orbital is referred to as π - π^* transition. The anti-bonding orbital is designated by an asterisk. For instance, 1,3-butadiene has an intense absorption band at 217 nm (usually written as λ_{max} 217 nm, i.e. wavelength of maximum absorption)



This results from the excitation of an electron from π_s to π_s^* . α , β -Unsaturated carbonyl compounds have absorption that resembles the corresponding dienes. Such spectra are interpreted in the same manner as transition of an electron from π_s to π_s^*



λ_{max} 240 nm ($\pi \rightarrow \pi^*$) and 319 nm ($n \rightarrow \pi^*$)

As is evident from their structures, carbonyl groups have another absorption associated with the lone pair of electrons on the oxygen atom and such a transition is designated as $n \rightarrow \pi^*$. It generally occurs at longer wavelengths. In order to obtain useful information from the ultraviolet spectrum of a compound, the λ_{max} and the intensity of absorption must be measured accurately. Absorption intensity is expressed in terms of the molar extinction coefficient defined by the ratio of the logarithm of the incident light intensity and the transmitted light intensity is proportional to the number of molecules in the light path. Expressed mathematically

$$\log I_0/I = \epsilon Cl = A$$

where I_0 is the intensity of incident light; I intensity of transmitted light; c molar concentration of the sample; l length (in centimetres) or the path of light beam that passes the sample cell; ϵ molar extinction coefficient; and A observed absorbance at a particular wavelength.

The molar absorptivity also referred to as the molar extinction coefficient relates the observed absorbance A to c and l . The magnitude of molar extinction coefficient for a particular absorption is directly proportional to the probability of the particular electronic transition. On irradiation with ultraviolet light the more probable a given transition the larger the extinction coefficient.

The compound is usually dissolved in some suitable solvent that itself does not absorb light in the region under investigation. The most suitable solvent in uv spectral determination is 95% ethanol. The modern spectrometer is designed to record the spectrum of light and consists of (1) a light source (2) monochromator (3) sample cell (4) photoelectric amplifier and (5) a recorder. The spectrum is obtained in the form of a graph which is a plot of the absorbance of light at each wavelength *versus* the wavelength of absorption.

A few terms, usually used in the discussion of electronic spectra may be described here. If a functional group which is not in conjugation with any other group exhibits absorption in the uv region, it is termed as a *chromophore*. A group that does not absorb itself is called an *auxochrome*. A shift of absorption to a longer wavelength, due to substitution or solvent effect, is called the *bathochromic shift* and a *hypsochromic shift* involves absorption to a shorter wavelength.

6.9.2 Infrared Spectroscopy

Organic compounds absorb light energy in the visible and in the uv region of the electromagnetic spectrum. Organic molecules also absorb energy in the infrared region of the spectrum, but infrared radiation does not have adequate energy to cause excitation of the molecule, instead it causes the atoms and groups of organic molecules to vibrate along the covalent bonds that link them together. Since the vibrations are quantized the molecules absorb infrared energy in particular region of the spectrum.

The operation of the infrared spectrometer is similar to the ultraviolet spectrometer. A beam of radiant light is passed through the sample and the spectrometer plots the results as a graph indicating absorption *versus* frequency or wavelength. From the spectrum so obtained, the location of the infrared absorption band can be specified either in frequency units or wave numbers (ν) measured in reciprocal centimetres (cm^{-1}) or by its wavelength (λ) measured in micrometres (μm).

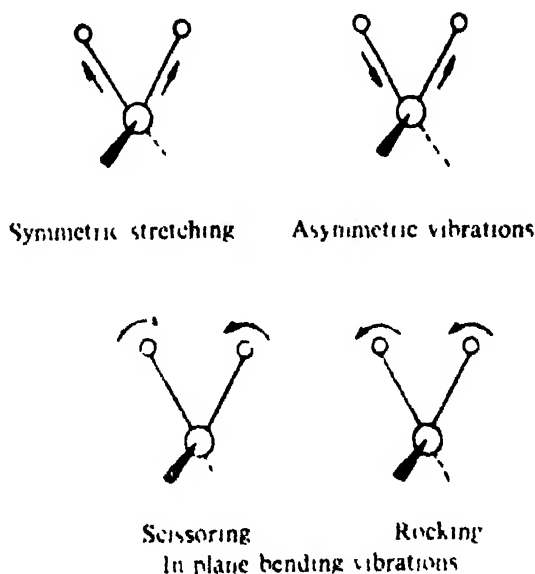
$$\nu = 1/\lambda \quad (\lambda \text{ in cm})$$

or

$$\bar{\nu} = 10,000/\lambda \quad (\lambda \text{ in } \mu\text{m})$$

The frequency of absorption depends on the relative masses of the atoms, the force constants of the bonds and the geometry of the atoms. A molecule is not rigid, but can vibrate in a number of ways. A molecule can be considered as resembling balls of different masses corresponding to the atoms in the molecule and springs of varying strengths corresponding to the chemical bonds of the molecule. In a molecule, there are two kinds of vibrations: *stretching*, in which the molecule vibrates back and forth along the covalent bond and *bending*, in which the vibrations involve changes in bond angles. A non-linear molecule that contains n atoms has $3n - 6$ possible

fundamental vibrational modes that are responsible for the absorption of infrared light.



The precise location of bands corresponding to the two modes of vibrations, of course, depends on the structure of the entire molecule. All molecular vibrations do not occur in the absorption of energy. In order for a vibration to occur, the dipole moment of the molecule must change as the vibration occurs. Such modes of vibration, where a change in dipole moment occurs with vibration are known as *infrared active*. Thus symmetrical bonds of $C=C$ (ethylenes) and $C\equiv C$ (acetylenes) do not result in this absorption of infrared absorption in the stretching mode. The infrared spectrometer consists of (1) a source of radiation, (2) a cell containing the sample; (3) a photometer; (4) a monochromator; and (5) a detector. A common source of infrared radiation is a Nernst glower which is heated electrically. The cell is generally made of rock salt or potassium bromide as they are relatively transparent in the infrared radiation. Liquid samples are usually examined without a solvent. It is frequently desirable to determine the spectrum of a substance in solution, and for this purpose a number of solvents are available. Solids are dissolved in suitable solvents which exhibit as little absorbance as possible in the spectral region, such as CCl_4 , CS_2 , $CHCl_3$, etc.

The infrared spectrum of a polyatomic molecule consists of a large number of peaks and the spectrum affords a large amount of information as will be illustrated by some examples. Table 6.1 containing characteristic infrared absorption of functional groups will be quite helpful.

Table 6.1 Characteristic Infrared Absorptions of Functional Groups

Functional Group	μ (10^{-6} cm)	Range (cm^{-1})
C—H (alkane, $-\text{CH}_3$)	3.38-3.51	2962-2853
C—H $\left[\begin{array}{c} \text{alkene, } \text{C} \begin{array}{c} \text{H} \\ \diagup \\ \text{C} \\ \diagdown \\ \text{H} \end{array} \end{array} \right]$	3.29-3.32	3040-3020
C—H (alkyne, $-\text{C}\equiv\text{C}-\text{H}$)	3.03	3300
C—H (aromatic)	3.30	3030
O—H (monomeric alcohols, phenols)	2.74-2.87	3650-3590
O—H (hydrogen bonded)	2.77-3.12	3600-3200
N—H (amines)	2.86-3.02	3500-3300
$\begin{array}{c} \quad \\ -\text{C}-\text{C}- \end{array}$ (alkene)	5.95-6.17	1680-1620
$-\text{C}\equiv\text{C}-$ (alkyne)	4.57-4.76	2260-2100
$-\text{C}=\text{C}-$ (aromatic)	6.25-6.67	1600-1500
$-\text{C}-\text{N}$ (amines, amides)		
$\text{C}-\text{O}$ (alcohols, carboxylic acids, esters)	7.96-9.52	1300-1050
$\text{C}=\text{O}$ (aldehydes, ketones, carboxylic acid esters)	5.68-5.97	1760-1690
$\text{C}-\text{O}$ (carboxylic acids)	5.80-5.98	1725-1750
$\text{C}-\text{O}$ (esters)	5.71-5.76	1750-1715
$\begin{array}{c} \text{H} \\ \\ -\text{C}-\text{O} \end{array}$ (aldehydes)	5.87-5.95	1705-1680
$\begin{array}{c} \\ -\text{C}=\text{O} \end{array}$ (ketones)	5.80-5.87	1725-1705
γ -Lactone	5.62-5.68	1780-1760
NO_2	6.37-6.67	1760-1690
$-\text{C}\text{I}$	12.5-16.6	800-600
$\text{C}-\text{Br}$	16.6-20.0	600-500
$\text{C}-\text{I}$	20	500
$\text{S}-\text{H}$	3.82-3.92	2600-2550

Interpretation of spectra: An infrared spectrum is a plot of wavelength (in) or frequency (wave number) as abscissa and a function measuring the

absorption of the compound at various wavelengths as ordinate. This function is the percent transmittance, i.e. $I/I_0 \times 100$, where I is the intensity of light passing through the sample and I_0 is the intensity of the incident light. The regions of maximum absorption therefore, appear as *valleys* in the spectrum. An infrared spectrum is usually complex because of the multitude of vibrations that can occur in a molecule containing several atoms and bonds. The interpretation of the spectrum commences with the examination of the major bands (see Table 6.1). The region extending from 7μ to 11μ is often referred to as the *fingerprint region* of the spectrum. It is characteristic and unique for every compound and in this region, the spectra of two dissimilar compounds differ. Only if the spectra of two organic compounds are completely superimposable does it indicate the two organic molecules are identical. Comparison of the spectra of unknown compounds with those of known compounds can thus be a very useful technique for identification of the unknown compound.

Let us consider the spectrum of 2-butanol. $\text{CH}_3\text{CHCH}_2\text{CH}_3$
 $\quad\quad\quad |$
 $\quad\quad\quad \text{OH}$

It shows absorptions owing to C—O and O—H stretching vibrations at 1120 cm^{-1} (8.92μ) and 3350 cm^{-1} (2.98μ) respectively, in addition to the

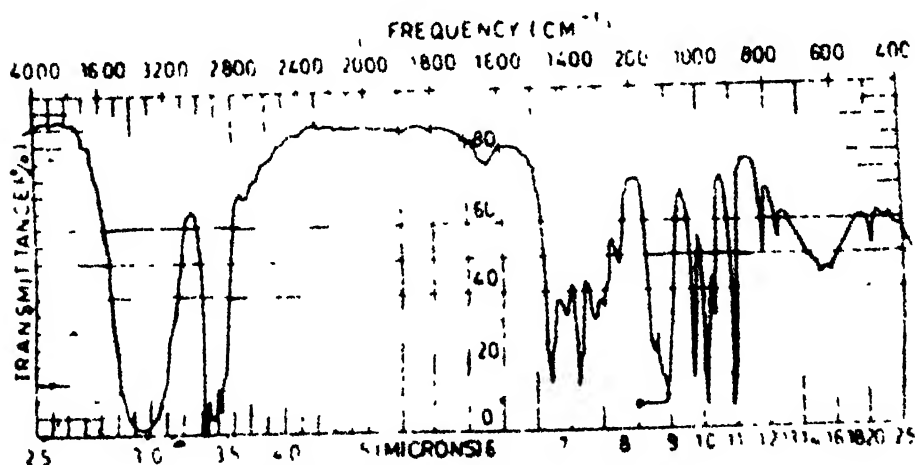


Fig. 6.3 Infrared Spectrum of 2-butanol

hydrocarbon chromophoric groups present. The strong absorption at 3350 cm^{-1} (2.98μ) is typical of the polymeric association of hydroxy groups. The non-bonded hydroxyl absorption peak is barely perceptible. If the infrared spectrum is run as a very dilute solution in carbon tetrachloride the hydroxyl group stretching frequency is shifted to higher frequencies, due to reduced intermolecular hydrogen bonding.

Figure 6.4 represents a spectrum of cyclohexanone $\left(\text{C}_6\text{H}_{10}\text{O}\right)$

The $\text{C}=\text{O}$ stretching frequency appears at 1715 cm^{-1} (5.83μ). The position of maximum absorption is sensitive to the ring size and to the degree of conjugation.

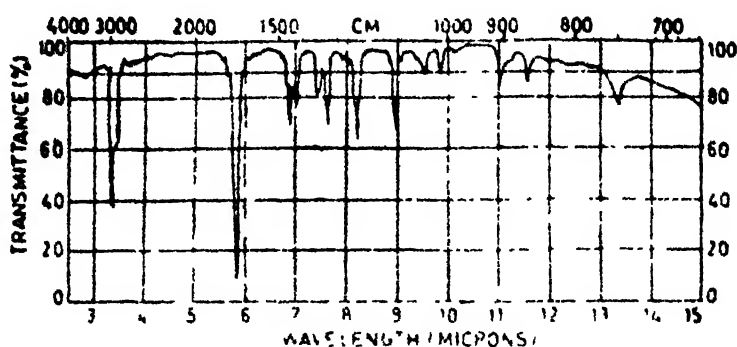


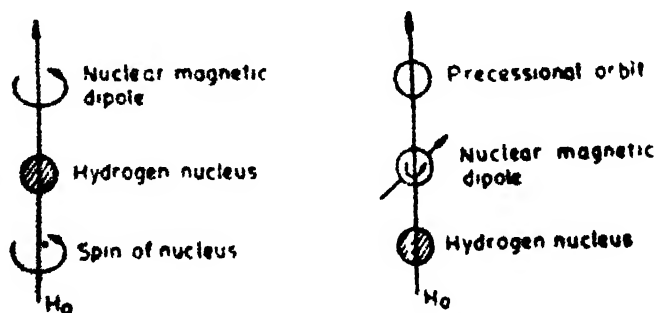
Fig. 6.4. Infrared Spectrum of Cyclohexanone

Thus, in cyclopentanone, the $\text{C}=\text{O}$ group absorbs at 1751 cm^{-1} (5.71μ) i.e., at a higher wave number. In case of conjugation absorption occurs at a lower wave number for example, in methyl tollyl ketone, the $\text{C}=\text{O}$ group absorbs at 1675 cm^{-1} (5.95μ).

6.9.3 Nuclear Magnetic Resonance Spectroscopy

The absorption of radio-frequency radiation by the nuclei of atoms is termed as *nuclear magnetic resonance* (nmr) and this technique has proved to be a powerful tool for structural studies. As the name implies, this form of spectroscopy depends on the magnetic properties of the nucleus of an element.

All nuclei carry charge and mass but nuclei of certain atoms also possess nuclear spin. A hydrogen atom, for instance, having one proton and one neutron each in the nucleus, has a spin number $I = 1/2$. This spinning nucleus, may be envisaged as a spinning top with an axis passing through the center, behaves like a tiny magnet and has magnetic moment.



Spinning of a nucleus in a magnetic field .

When a compound containing hydrogen (protons) is placed in an external magnetic field, H_0 , the protons may assume one of two possible orientations given by $(2I+1)$ the two orientations with respect to the external magnetic

field; the number of orientations being given by $2I + 1$. For nuclei with $I = 1/2$ as in the case of ^1H , ^{13}C , ^{19}F , etc., the orientations are two, one aligned with the field and the second against the applied field. This is shown in the following diagram.

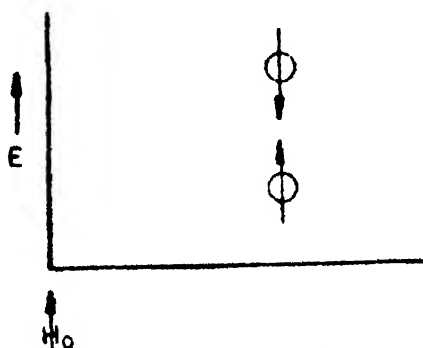


Fig 6.5 Energy Levels of a Proton

The former orientation is in a state of low energy while latter that of a high energy. The axis of the spinning proton, under the influence of the external field, precesses about the axis of the applied field. The frequency, ω_0 of precession is given by

$$\omega_0 = \gamma H_0 = 2\pi\nu_0$$

where γ is a constant known as the magnetogyric ratio (a fundamental nuclear constant) and ν_0 is the frequency of precession. The frequency ω_0 thus increases as H_0 increases. If electromagnetic radiation of frequency ν is applied at right angles to the applied field, the applied frequency is said to be in *resonance* with the precessional frequency when $\nu = \nu_0$. At this stage the radiation is absorbed by the nucleus and it undergoes a 'flip' from its lower energy state to the higher energy level. An absorption peak is obtained, which can be detected electronically and recorded as a peak on a chart. This is achieved experimentally by applying resonance frequencies which in the case of a proton are in the radio frequency range, i.e. electromagnetic radiation of 60×10^6 cycles/second or 60 MHz (mega Hertz) and corresponds to a wavelength of 5×10^2 cm in a magnetic field of 140,92 gauss the value of H_0 . The condition for resonance of a proton can be achieved either by holding H_0 constant and varying ν or by maintaining ν at a constant value and changing H_0 . The latter approach, however, is more convenient.

Nuclei that have spin and are important to an organic chemist are ^1H , ^{13}C , ^{19}F etc. Most nmr studies have been carried out on the hydrogen (proton) nuclei and the technique is thus referred to as *proton magnetic resonance* (pmr).

In an nmr spectrum, an absorption peak is obtained for each type of different proton in the molecule at different frequencies of resonance. This depends on the environment in which the nuclei exists, i.e. the neighbouring atoms. A proton in a molecule is surrounded by a cloud of electronic charge

whose density varies with the environment. In a magnetic field, the electrons will circulate and generate their own magnetic field that ordinarily opposes the applied field. As a result the nucleus is exposed to an effective field that is somewhat smaller (but in some cases larger too) than the external field. In other words, the net magnetic field is slightly less than the applied field. Since the nucleus or the proton experiences a smaller field, it is said to be *shielded* by the electrons. The degree of shielding of a proton depends on the density of the circulating electrons and in the case of proton, it depends on the inductive effect of the group attached to the carbon atom carrying the proton. In order to circumvent the deshielding effects, a higher magnetic field must thus be applied to achieve resonance. This gives rise to a *chemical shift*, which is described as the difference in the absorption position of a particular proton of a sample from that of the reference proton. There are several types of reference compounds but for protons, the position of the absorption peak is noted with reference to tetramethylsilane, TMS $[(CH_3)_4Si]$, a volatile liquid, b.p. $-26.5^\circ C$ used as an internal standard. For this compound a single sharp resonance line occurs at a position, where it is unlikely to obscure peaks arising from the sample. This standard is assigned a chemical shift of 0 Hz. The circulation of delocalized π electrons generates magnetic fields that can either *shield* or *deshield* neighbouring protons in the molecule. The occurrence of *shielding* or *deshielding* depends on the location of protons in the *induced* field. The aromatic protons of benzene derivatives are *deshielded* because their locations are such that the induced magnetic field reinforces the applied magnetic field. Due to this deshielding, the chemical shift values of hydrogen atoms attached to an aromatic ring is usually greater than protons in hydrocarbons.

The chemical shift of a proton is determined in terms of cycles per second depending upon the oscillator frequency. It has been found convenient to convert such shifts into units independent of frequency expressed as delta (δ)

$$\delta = \frac{\text{Chemical shift in cps}}{\text{Oscillator frequency of the instrument in cps}} \times 10^6$$

The δ values are expressed as parts per million (ppm) and do not depend upon the frequency of applied radiations. An alternative scale is the *tau* (τ) scale, for which TMS is assigned an arbitrary value of 10 000. To convert a chemical shift given on the delta scale to a value on the tau scale, one simply subtracts the shift as measured on the delta scale from 10 000, i.e. $\tau = 10\,000 - \delta$. The chemical shifts for a wide variety of hydrogen atoms in different environment is given in Table 6.2.

The nmr instrument allows chemists to measure the absorption energy of hydrogen nuclei. These instruments use very powerful magnets and irradiate the sample with electromagnetic radiation in the radio frequency region. The sample is mixed in a glass tube whose internal diameter is 2-3 mm. A few drops of TMS is then added and the tube is then placed in the sample holder between the pole faces of a dc electromagnet spaced 1.75 inches apart.

Table 6.2. Typical Chemical Shifts of Hydrogens

Type of Hydrogen	Chemical shift	
	(τ)	(δ ppm)
RCH_3	9.1	0.9
R_2CH_2	8.7	1.3
R_3CH	8.5	1.5
$\text{C}=\text{C}-\text{H}$	4.1-5.4	4.6-5.9
$\text{Ar}-\text{H}$	1.5-4	6-8.5
$\text{C}=\text{C}(\text{H})_2$	8.2	1.7
$\text{C}(\text{H})=\text{CH}_2$	5.3	1.8
$\text{Cl}-\text{CH}$	6.7	3.3
Cl_2CH	4.2	8
$\text{Br}-\text{C}(\text{H})$	6.7-5	2.5-4
$\text{O}_2\text{N}-\text{CH}$	4-5.5	4.2-4.6
$\text{OC}(\text{H})$ (alcohol, ether)	6-6.7	3.3-4
$\text{OC}(\text{H})$ (esters)	5.2-6.4	3.7-4.1
$\text{O}-\text{C}(\text{H})-\text{H}$	7.3-5	2.2-2.7
$\text{R}-\text{C}(\text{H})-\text{H}$	0.1	9.10
$\text{RO}-\text{H}$	4.0	1.5-5
$\text{Al}-\text{OH}$	2 to 4	4-12
$\text{R}-\text{C}(\text{H})-\text{OH}$	4.0-10	10-5
RNH_2	5.0	5
$\text{N}-\text{C}(\text{H})-\text{H}$	0.1	10.1

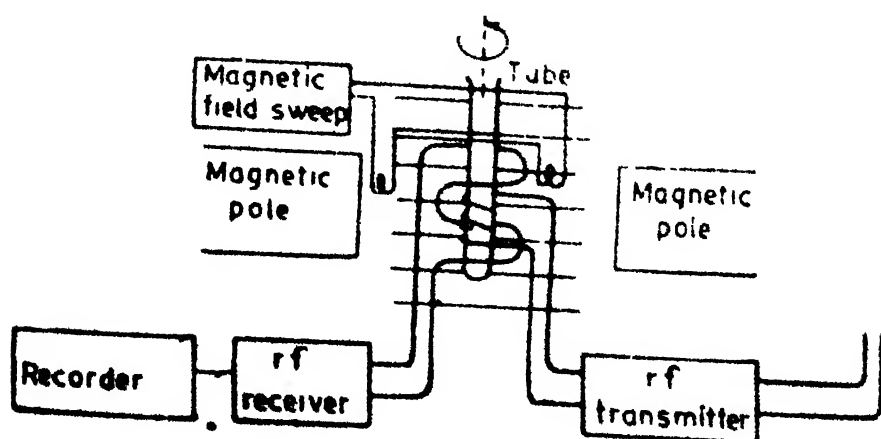


Fig. 6.6 Diagram of a Nuclear Magnetic Resonance Spectrometer

The radio frequency signal produced by the resonating nuclei is detected by means of a coil that surrounds the sample. The sample holder is rotated

which serves to average out the effects of inhomogenities; sharper lines are obtained as a consequence.

Interpretation: Let us consider the spectrum of anisole to demonstrate the utility of the nmr technique. The hydrogens of the $-\text{OCH}_3$ group are chemically equivalent, thus a single peak appears at 6.92 τ . The signals downfield are those of the aromatic ring. The *ortho* protons being closer to the $-\text{OCH}_3$ group are more shielded than the *meta*- and *p**ara*-protons. After the spectrum is determined it is integrated to estimate the relative number of protons in each absorption peak. The integral tracing is recorded from left to right. The height to which the tracing rises in the peak region for each group of protons, is proportional to the area enclosed by each peak, and also proportional to the number of protons responsible for that peak.

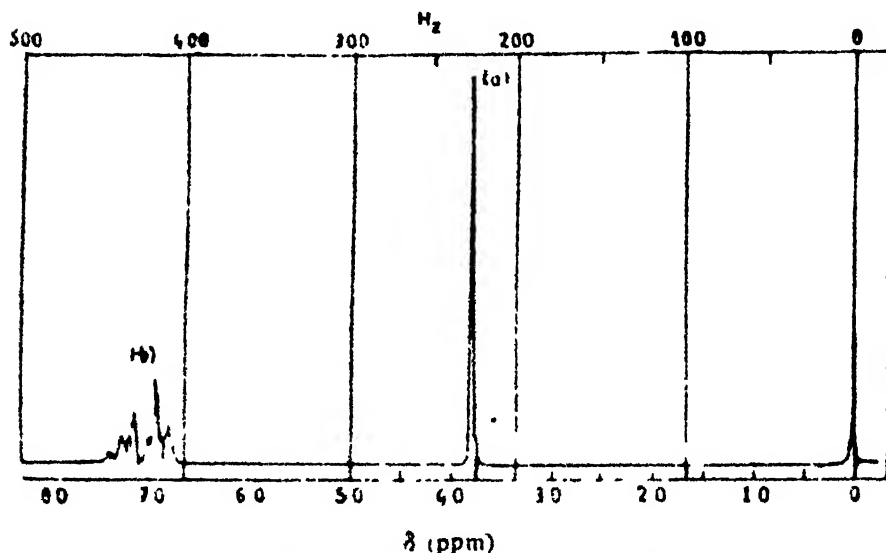
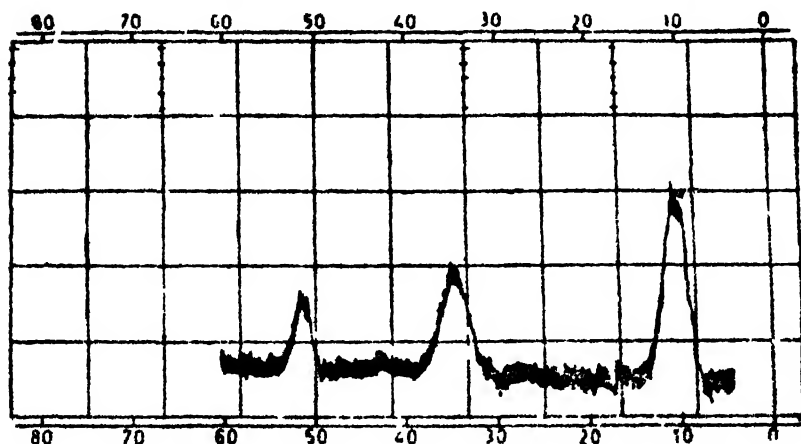


Fig. 6.7 NMR Spectrum of Anisole

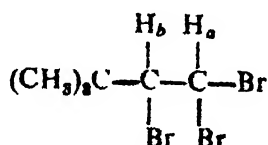
As is evident from the structure of ethanol it contains three types of protons and they absorb at different τ values and correspond to $-\text{OH}$ (4.63 τ), $-\text{CH}_2$ (6.38 τ) and $-\text{CH}_3$ (8.83 τ) protons. The area of each peak corresponds to a numerical ratio of 1: 2: 3.

The nmr is a convenient measure of not only the type but also the number of different protons in a molecule.

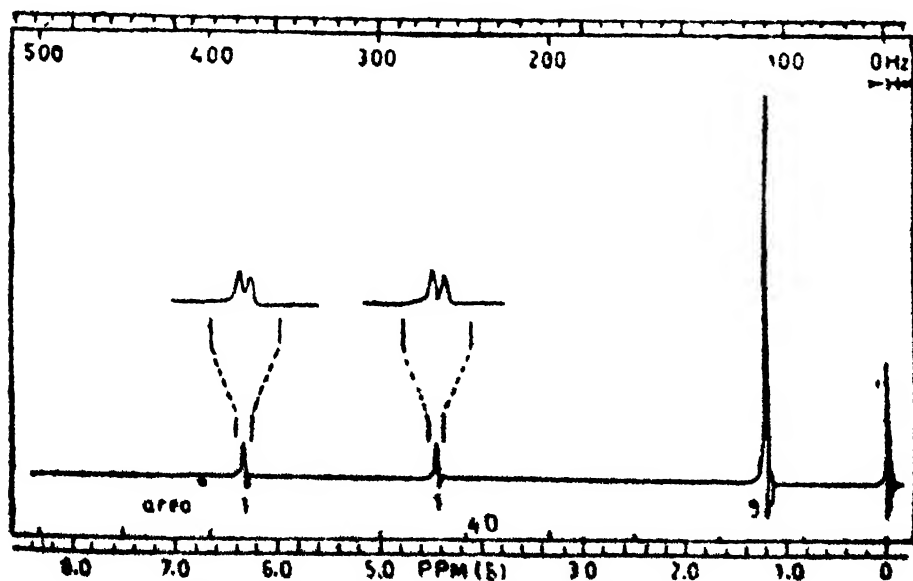
Spin-spin splitting: We have noticed that in an nmr spectrum, a series of peaks is obtained, representing proton in different chemical environments. The neighbouring group or atom influences the electron density and the resultant magnetic field around a proton and hence can cause significant shift in the signal. Such a signal, however, is influenced by the spin states of the neighbouring protons, resulting in its splitting. This arises from a phenomenon known as *spin-spin coupling*. This happens because of the tendency of a bonding electron to pair its spin with the spin of the nearest proton, the spin of a bonding electron having been thus influenced, the electron will affect the

Fig. 6.8 NMR Spectrum of Ethanol ($\text{CH}_3\text{CH}_2\text{OH}$)

other bonding electron and so on. Let us for instance, consider the two protons H_a and H_b in 3,4,4-tribromo-2,2-dimethylbutane ($(\text{CH}_3)_2\text{CCHBrCHBr}_2$)



Each proton will give rise to an absorption peak but the spin of each proton is affected to some extent by the two orientations of the other proton through the intervening bonds so that the signal of each proton is split into two and appears as a doublet of equal intensity. This actually is observed in practice as is evident from the spectrum.

Fig. 6.9 NMR Spectrum of $(\text{CH}_3)_2\text{CCHBrCHBr}_2$



The distance between the split peaks is usually denoted by J and is called the *coupling constant*. It is reported in Hertz (cycles per second). Coupling constant is a measure of the effectiveness of coupling between two protons with different chemical shifts. It is a definite quantity and varies with structure but is independent of the applied field.

We do not observe spin-spin splitting if the protons affecting each other are chemically equivalent. Thus we would not expect signal splitting in the signal from the six equivalent hydrogens of ethane.

If the spectrum of acidified ethanol is recorded under high resolution, it is found that the peaks are split.

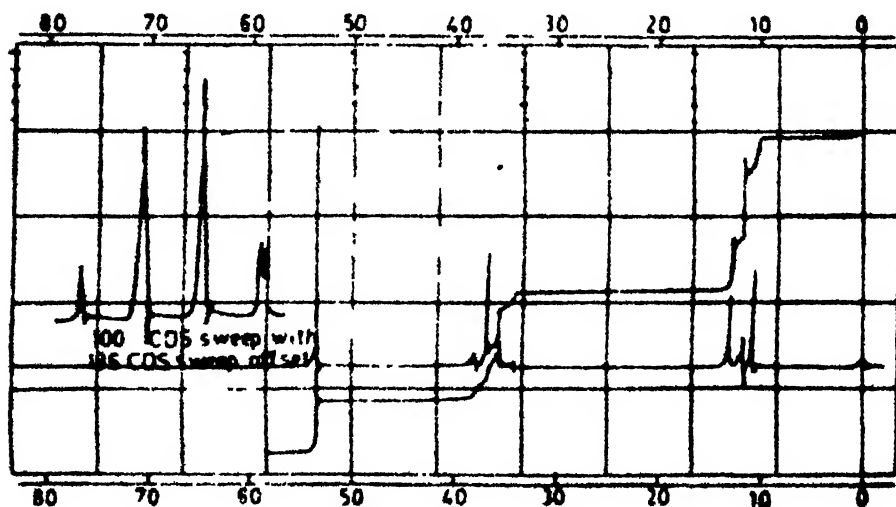
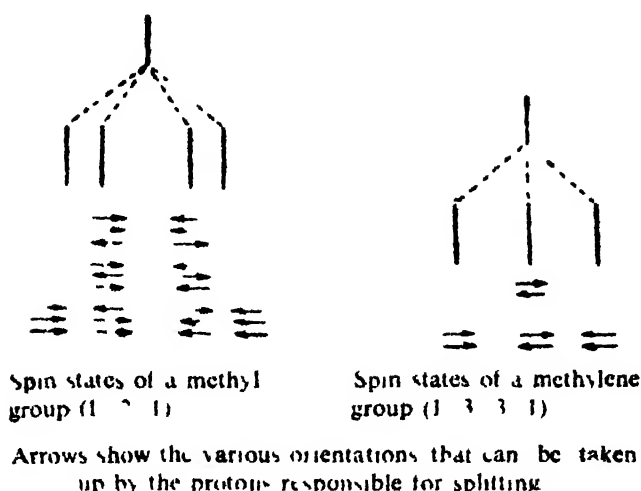


Fig. 6.10 NMR spectrum of Ethanol under High Resolution

The methyl group is split into a triplet of intensity (1 : 2 : 1) and the methylene group into a quartet of intensity (1 : 3 : 3 : 1). The spectrum of pure ethanol, however, is more complicated. Broadly speaking, the observed multiplicity of a given group of equivalent protons is given by $(\gamma + 1)$, where γ represents the number of protons on the neighbouring carbon atom. The splitting pattern of proton signals can furnish very valuable structural information.



QUESTIONS

- 6.1 Describe the principle involved in the estimation of nitrogen.
- 6.2 a Explain the various techniques for the purification of a liquid.
b If a liquid distils at constant temperature, can an inference be drawn that it is pure?
- 6.3 Chromatographic methods have been considered as the most viable techniques for the separation and purification of compounds. Discuss the different chromatographic techniques.
- 6.4 Predict the elution sequence of a mixture of compounds containing chlorobenzene, *p*-cresol and anthracene developed on an alumina column using a solvent system of progressively increasing polarity.
- 6.5 A sample containing 0.45 g of an organic compound, gave on combustion 0.72 g of CO_2 and 0.324 g of H_2O . Another 0.24 of this substance was Kjeldahlized and the ammonia evolved was absorbed in 50 ml of $\text{N} \cdot 4 \text{H}_2\text{SO}_4$. The excess acid required 77.0 ml of 0.1N NaOH for complete neutralization. Calculate the empirical formula of the compound.
- 6.6 A 0.2 g sample of an organic monobasic acid gave on combustion 0.505 g of CO_2 and 0.089 g of H_2O ; 0.183 g of the acid required 15 ml of 0.1N NaOH for complete neutralization. Calculate the molecular weight and the molecular formula of the acid.
- 6.7 A compound on analysis gave C = 54.55%, H = 9.09%, and O = 36.26%. Its vapor density is 44. Find the molecular formula.
- 6.8 A monobasic acid gave the following data on combustion, 0.419 g of the acid 1.058 g of CO_2 and 0.185 g of H_2O , and 0.470 g of the silver salt of the acid produced on ignition 0.222 g of silver. Calculate the molecular formula of the acid.
- 6.9 Elemental analysis of an organic compound gave C = 39.98%, H = 6.72%, and O = 53.3%, and 0.151 g of the compound on vaporization

displaced 33.8 ml of air measured at 25° over water and at a pressure of 745 mm of Hg. Determine its empirical and molecular formula, given that the vapor pressure of water at 25° is 24 mm Hg.

- 6.10 A monoacid base contains C = 53.3%, H = 15.5% and N = 31.2%. One gram of the chloroplatinate salt of the base gave 0.32 g of platinum on ignition. Calculate its molecular formula.
- 6.11 A compound A, $C_7H_{15}N$, is insoluble in water but dissolves in dil. hydrochloric acid. A undergoes no reaction with nitrous acid. When A is treated with methyl iodide and then with silver oxide, B is formed. On heating, B forms C, $C_8H_{17}N$. C, adds hydrogen in the presence of a catalyst forming D, $C_8H_{19}N$. D, on treatment with methyl iodide and then with silver oxide yields $(CH_3)_3N$ and E. E can be hydrogenated to 2-methylpentane. Assign structures to compounds A to E.
- 6.12 Compound A, $C_{10}H_{20}O_3$, is not soluble in water or in sodium bicarbonate. It gives no reaction with $C_6H_5NHNH_2$. Refluxing of A with sod. hydroxide solution, extraction of the mixture with ether and evaporation of the solvent yields B, $C_8H_{12}O$. Acidification of the NaOH solution forms a new compound C, $C_8H_{10}O_2$ which is optically active. B gives a positive iodoform test. Suggest structures for A, B and C.
- 6.13 Two compounds A and B each containing C = 63.58%, H = 5.96%, and N = 9.26% give benzoic acid on oxidation. Both dissolve in NaOH solution with a red coloration. On reduction A and B yield amines C and D respectively. C, but not D, can be resolved into optical isomers. What are A and B?
- 6.14 An organic compound A, contains C = 76.6%, H = 6.38% and gives a mixture of two isomers B and C when an alkaline solution of A was refluxed with chloroform at 60°. B, being steam volatile was separated by steam distillation which on oxidation gives an acid D, containing C = 60.67%, H = 4.34%. The acid D was also obtained by heating sodium salt of A at 125-140° under pressure. Assign structural formulae to the lettered compounds.
- 6.15 A compound of formula, $C_4H_{10}O$, reacts rapidly with metallic sodium but not with Lucas reagent. Treatment of A, with hot conc. sulfuric acid yields a new compound B, C_4H_8 . If B is hydrated with aqueous sulfuric acid, a new compound C, $C_4H_{10}O$ is formed. Compound C is almost inert to metallic sodium but reacts rapidly with Lucas reagent. Assign structures to A, B and C.
- 6.16 An organic compound A, $C_8H_{16}O$, does not react with sodium. On treatment with HI, it yields two compounds B and C. B reacts with sodium to liberate hydrogen and also forms a salt with sodium hydroxide. B can also be brominated and the major product contains two bromine atoms. The compound C contains iodine. On treatment with magnesium in ether, followed by CO_2 , it forms acetic acid. What are A, B and C?

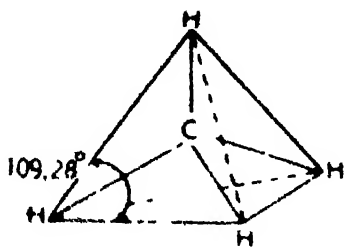
- 6.17 An alkene A, on ozonolysis yields acetone and an aldehyde. The aldehyde is easily oxidized to an acid B. When B is treated with bromine in the presence of phosphorus, it yields a compound C which on hydrolysis gives a hydroxy acid D. This acid can also be obtained from acetone by reacting it with hydrogen cyanide followed by hydrolysis. Identify the compounds A, B, C and D.
- 6.18 An organic compound contains C = 81.55%, H = 4.85% and N = 13.6% and has a vapor density of 51.5. It evolves ammonia when heated with KOH and reduction with sodium and alcohol forms a base which reacts with nitrous acid giving off nitrogen and yielding alcohol. This alcohol can be oxidized to benzoic acid. What is the original substance? Explain the above changes.
- 6.19 An aromatic monobasic acid A, contains C = 70.6% and H = 5.71%. Its methyl ester has a V.D. of 75. When A is distilled with soda lime it gives a hydrocarbon. On oxidation with KMnO_4 it gives a dibasic acid B. Name the compound and four of its isomers. How will you distinguish between these isomers?
- 6.20 A compound R, with molecular formula $\text{C}_8\text{H}_{10}\text{O}$ is insoluble in dil. acid and base. It does not reduce Tollens reagent but forms a 2, 4-dinitrophenylhydrazone. On vigorous oxidation an acidic product $\text{C}_8\text{H}_6\text{O}_4$ is formed which forms an acid anhydride on heating. Treatment of R with sodium hypobromite gives a different acid which, when heated with soda-lime, yields toluene. Propose a structural formula for R.
- 6.21 An organic compound A, contains C = 90.56%, and H = 9.43%. Its vapor density is 53. On oxidation A yields a dibasic acid (B) containing 57.8% C and 3.6% H. The silver salt of the acid contains 56.8% of silver. The acid, on heating, forms a compound C of molecular formula $\text{C}_8\text{H}_4\text{O}_3$. On distillation with soda lime, the acid forms benzene. Explain the above reactions and assign structural formulae to A, B and C.
- 6.22 An organic compound A contains C = 68.85%, H = 4.9% and reacts with NH_4OH ; on treatment with NaOH, it forms two compounds B and C. The compound B is soluble in HCl and can be oxidized to compound C with alkaline KMnO_4 . The compound C on treatment with conc. HCl forms an acid D, which on heating with an alkali gives phenol. Identify the compounds A, B, C, and D. Explain and name the reactions.
- 6.23 An organic halogen compound A which contains C = 66.41%, H = 5.53% and Cl = 28.04% on treatment with potassium hydroxide solution gave a hydroxy compound B, containing C = 77.77%, H = 7.40% but no halogen. B, on oxidation yields a monobasic acid C, which on distillation with soda lime gave benzene. Assign structures to A, B and C and describe a method for the preparation of compound A.

- 6.24 A 1.06 g sample of an organic compound gave on combustion 3.08 g of CO_2 and 0.54 g of H_2O . Its vapor density is 23. This compound on heating with caustic soda yields an alcohol and the sodium salt of an acid. Distillation of the sodium salt of the acid with soda lime gives benzene. Determine the structural formula of the compound, the alcohol and the acid.
- 6.25 An organic compound A, molecular formula $\text{C}_3\text{H}_8\text{O}_3$, when treated with excess ammonia and then heated formed B, molecular formula $\text{C}_3\text{H}_7\text{ON}$. B, when heated with P_2O_5 , formed C molecular formula $\text{C}_3\text{H}_5\text{N}$. C, on complete hydrolysis formed A. C, on reduction with a complex metal hydride formed a basic nitrogenous compound, D, molecular formula $\text{C}_3\text{H}_9\text{N}$. D, on treatment with nitrous acid formed an alcohol E, molecular formula $\text{C}_3\text{H}_8\text{O}$. E, on oxidation formed compound A. Give the structures of compounds A, B, C, D and E and explain the reactions.
- 6.26 A neutral solid A, has the formula $\text{C}_{10}\text{H}_7\text{O}_4\text{N}$. Vigorous oxidation of A gives a dibasic acid B, $\text{C}_8\text{H}_5\text{O}_6\text{N}$. A, can be reduced to a compound C, $\text{C}_{10}\text{H}_9\text{N}$ which on oxidation gives a dibasic acid D, $\text{C}_8\text{H}_5\text{O}_4$. The compound A, can be obtained by direct nitration of a particular aromatic hydrocarbon. Identify compounds A to D.
- 6.27 A compound A contains C - 48%, H - 4%. Sodium fusion of A reveals the absence of halogen, sulfur and nitrogen. What is the empirical formula of A?
- 6.28 A ketone 'A' undergoes haloform reaction, and on reduction gives a compound B. On heating with sulfuric acid B yields C which forms monooxozonide D with ozone. D on hydrolysis in the presence of zinc dust gives only acetaldehyde. Identify compounds A, B, C and write the chemical reactions involved.

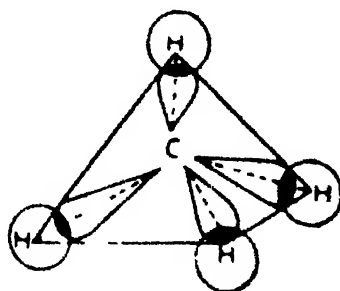
Alkanes or Paraffins

We will begin with the study of simple aliphatic organic hydrocarbons containing carbon and hydrogen, i.e. *alkanes*. These are saturated compounds and each carbon holds its maximum of four atoms or groups. These are also known as *paraffins*. They display stability towards many reagents. They occur naturally and natural gas is largely composed of methane (98%). Natural gas is extensively used as fuel both in domestic gas ranges and in industry. The putrefaction of cellulose in the absence of air also gives rise to methane and this often occurs in swamps (marsh gas). Thus natural gas and marsh gas are other names for methane. Petroleum is another source of these hydrocarbons. It furnishes gasoline, lubricating oils, vaseline and paraffin wax, tar, etc., all of which are rich in saturated hydrocarbons.

The general formula of alkanes corresponds to C_nH_{2n+2} or $C_nH_{2n+1}H$ or RH . The structures of the first member of the alkane family, namely methane is given below.



Tetrahedral structure of
Methane



Molecular orbital representation of
Methane

In methane the carbon-hydrogen bonds are formed by the overlap of carbon sp^3 hybridized orbitals with the hydrogen s -orbitals. The configuration of lowest energy is a tetrahedron with the four hydrogen atoms situated at the four corners. The bonds in methane subtend an angle of 109.28° and the $C-H$ bond distance is 1.09\AA .

The next higher member is ethane then propane, butane and so on. Notice that in the series methane CH_4 ; ethane C_2H_6 , and propane C_3H_8 , each molecule differs from the previous one by an additional unit of CH_2 . A group of molecules of this type each differing from the next by the unit CH_2 is said to comprise a *homologous series*, and compounds belonging to such a series are called homologs of one another. Members in a series are closely related in chemical properties and display a regular gradation in physical properties (Table 7.1). The first three members have no isomers, but isomerism commences from butane which exists in two isomers, i.e. chain isomers and



n-Butane

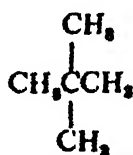


iso-Butane

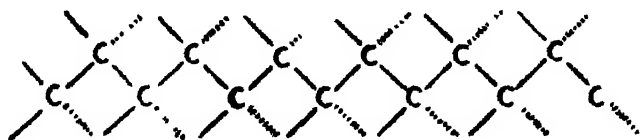
pentane has three. The number of isomers increases as the number of carbon atoms in the chain increases. Customarily the chain of saturated carbon



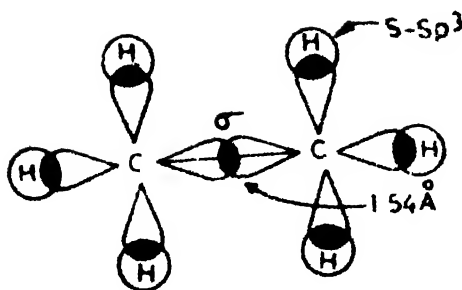
Pentane

Iso Pentane
(2-Methyl butane)neo Pentane
(2,2-Dimethyl propane)

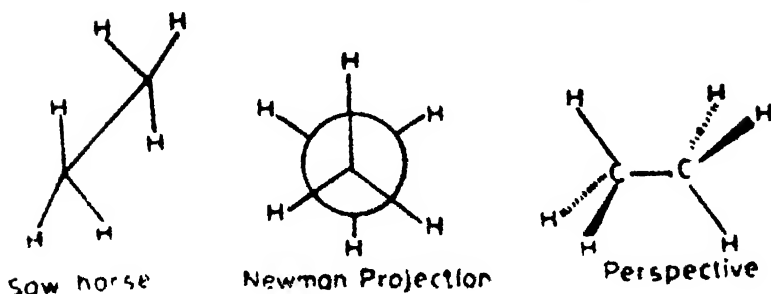
atoms is written for convenience in a straight line, but it may be remembered that the atoms are rather actually arranged in a zig-zag manner as shown below:



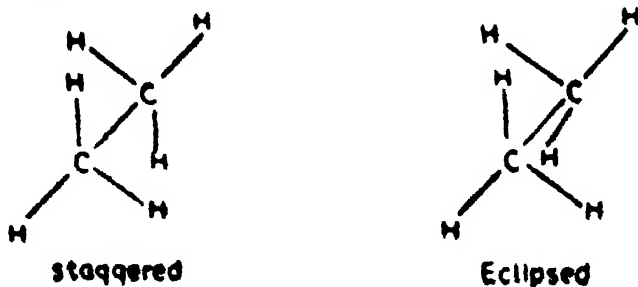
In ethane each carbon is tetrahedral, i.e. sp^3 hybridized. The two carbon atoms are bonded by the shared electrons in the molecular orbital created by the overlap of two sp^3 hybrid orbitals with the resultant formation of a carbon-carbon single bond or a σ -bond. The C—C bond distance is 1.5 Å. The bond in ethane is strong because the hybrid orbitals are directed in the right direction for an effective overlap. The carbon-hydrogen bonds are formed as in methane. The different three-dimensional representations for ethane are the following:



Molecular Orbital Representation of Ethane



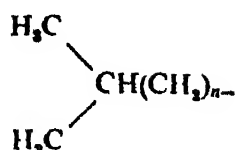
The two $-\text{CH}_3$ groups joined by the single $\text{C}-\text{C}$ bond are free to rotate with respect to each other. An important implication of this rotation is that the organic molecules have freedom to twist and attain a number of conformations. The two conformations of ethane namely *staggered* and *eclipsed* are shown below:



7.1 NOMENCLATURE OF ALKANES

The rules of nomenclature are adequately described in Sec. 2.3. Certain additional points may also be noted here. If a side chain or branch consists only of carbon and hydrogen atoms linked by single bonds, it is called an *alkyl* group. The name is derived by changing the ending *-ane* to *-yl*. This change is the key to making up names for alkyl groups. The carbon atoms are classified as primary, secondary and tertiary depending on whether the carbon atom is attached directly to one, two or three other carbon atoms.

The prefix *iso* has a special meaning. It can be used to name a group containing the following feature:



where $n = 0, 1, 2, 3, \dots$. $n=0$, *iso*-propyl; $n = 1$, *iso*-butyl; $n = 2$, *iso*-pentyl; $n = 3$, *iso*-hexyl

7.2 PHYSICAL PROPERTIES OF ALKANES

The physical properties of a molecule usually refer to its bulk properties without carrying out a chemical reaction. Some of the physical properties of a molecule are its physical state, melting point, boiling point, density, refractive index, solubility, etc. These properties are very much dependent on the structure of a molecule. The alkanes are less dense than water and oil floats on water. The viscosity increases with increasing molecular weight.

Melting Point Ions or molecules in a crystalline solid are arranged in a regular geometric fashion. Melting occurs when a temperature is reached at which the thermal energy of the particles is great enough to overcome the intercrystalline forces that hold them together. During melting, the ordered crystal structure is destroyed. The melting point reflects the strength of the intermolecular forces in a crystal. The more symmetrically built is the crystal of a compound the more firmly it is packed and higher is its melting point. Ionic compounds have much higher melting points than the non-polar organic molecules due to their stronger ionic bonds. The melting points increase gradually in the alkane series, as is evident from Table 7.1.

Table 7.1 Physical Properties of Straight Chain Alkanes

Hydrocarbon	Formula	No. of Isomers	Melting Point (°C)	Boiling Point (°C)	Density
Methane	CH_4		182.5	-161.7	
Ethane	C_2H_6		183.3	-88.6	
Propane	C_3H_8		-187.7	-42.1	
Butane	C_4H_{10}	2	-138.3	-0.5	0.5767
Pentane	C_5H_{12}	3	129.8	36.1	0.5572
Hexane	C_6H_{14}	5	-95.3	63.7	0.6603
Heptane	C_7H_{16}	9	90.6	98.4	0.6837
Octane	C_8H_{18}	18	56.8	125.7	0.7026
Nonane	C_9H_{20}	35	53.5	150.8	0.7177
Decane	$\text{C}_{10}\text{H}_{22}$	75	29.7	174.0	0.7199
Undecane	$\text{C}_{11}\text{H}_{24}$	159	-25.6	195.8	0.7402
Dodecane	$\text{C}_{12}\text{H}_{26}$	355	-9.6	216.3	0.7487
Tridecane	$\text{C}_{13}\text{H}_{28}$	802	-5.5	235.4	0.7564
Tetradecane	$\text{C}_{14}\text{H}_{30}$	1858	5.9	253.7	0.7628
Pentadecane	$\text{C}_{15}\text{H}_{32}$	4347	10	270.6	0.7685
Eicosane	$\text{C}_{20}\text{H}_{42}$	336,319	36.8	343	0.7886
Pentacosane	$\text{C}_{25}\text{H}_{52}$	736 million	65.8	449.7	
triacontane	$\text{C}_{30}\text{H}_{62}$				
tetracontane	$\text{C}_{40}\text{H}_{82}$				

Boiling Point: In a liquid, the particles are not arranged in a regular manner and are thus free to move. A liquid boils when a temperature is reached at which the thermal energy of the particles is great enough to overcome the cohesive forces that hold them together. An ionic compound has a high boiling point because it requires a high energy to break away ions, the constituent of the salt, in comparison to a liquid. Interaction between neutral molecules results from van der Waals forces, hydrogen bonding and dipole-dipole interactions. These forces hold molecules in a liquid together, but are very weak, thus boiling of a non-polar compound occurs at a very much lower temperature.

Alkanes are constituted of carbon and hydrogen atoms and are non-polar and only van der Waals interactions are important. The first four members of the alkane series are gases at room temperature, but as one ascends the series starting from *n*-pentane, which is a liquid at room temperature, each additional CH_2 group corresponds to an approximate rise of 25° to 30° in the boiling point of each homologue. As the complexity of the molecule increases its boiling point increases. In straight chain hydrocarbons, the molecules are packed closely together regularly and they have higher boiling point than the branched hydrocarbons (Table 7.2) since the latter fit

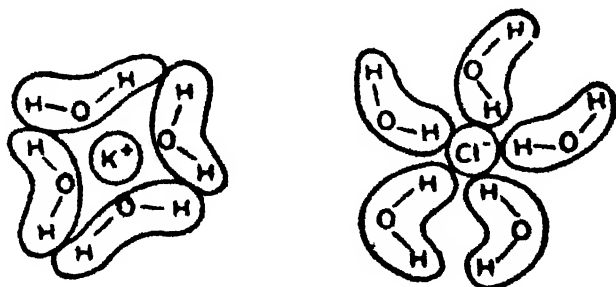
Table 7.2. Comparison of Physical Properties Between Straight Chain and Branched Hydrocarbons

Hydrocarbon	Melting Point ($^\circ\text{C}$)	Boiling Point ($^\circ\text{C}$)
<i>n</i> -Butane	-138	0
<i>iso</i> -Butane	-159	-12
<i>n</i> -Pentane	-130	36
<i>iso</i> -Pentane	-160	28
<i>neo</i> -Pentane	-17	9.5

into a symmetrical structure with great difficulty. The effect of branching on the boiling point is observed with all the homologous series of organic compounds. The reason is that with branching the shape of the molecule approaches that of a sphere and its surface area decreases, thus the intra-molecular forces decrease with the resultant decrease in the boiling point.

Solubility: The solubility of a molecule depends on several intermolecular forces such as ion-dipole, solvent-solute, solvent-solvent, etc. A compound dissolves in water if it can form hydrogen bonds with water. During dissolution of a solid or a liquid, the ions or molecules separate out and the

spaces in between them are taken up by the formation of new bonds between solvent and the solute particles. Dissolution of solid also involves the destruction of the ordered crystal structure. An ion in aqueous solution is surrounded by water molecules and is referred to as a solvated ion and the phenomenon is known as *solvation*. For an electrolyte, say KCl, during solvation an interaction takes place between the positive potassium ion and the negative-end of water molecules, and, between the negative chloride ion and the positive-end of water molecules as shown below:



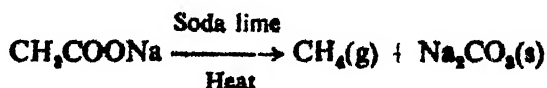
This is a case of the familiar generalization that *like dissolves like*, which implies that polar molecules are more soluble in polar solvents and non-polar molecules are more soluble in non-polar solvents.

The alkanes, being non-polar, are insoluble in polar solvents such as water, alcohol, acetone, etc. Methane is the most soluble among the paraffinic hydrocarbons, dissolving to the extent of 0.0025 g/100 ml of water. Alkanes with larger carbon chains are less soluble and it is generally true for organic compounds that the larger the carbon chain the less soluble it is in water. They are, however, soluble in non-polar solvents such as benzene or carbon tetrachloride.

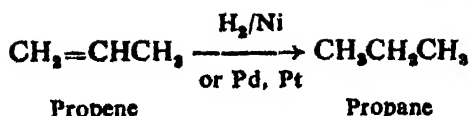
7.3 PREPARATION OF ALKANES

Lower alkanes are obtained from crude oil and are thus generally not prepared.

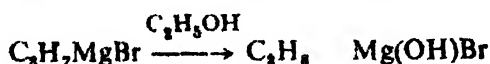
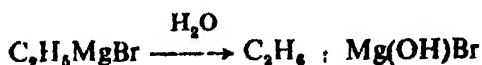
1. *Laboratory Preparation:* A laboratory preparation of methane may be demonstrated by heating sodium acetate in the presence of soda lime (a mixture of CaO and NaOH) in a test tube. Methane gas so evolved is collected.



2. *Hydrogenation of Alkenes:* Hydrogenation of alkenes in the presence of a catalyst is a useful method to obtain alkanes. Thus hydrogenation of propene with H_2 in the presence of Ni gives propane.



3. *From Grignard Reagents:* Alkyl halides (RX, where X = Cl, Br, I) react with magnesium metal under anhydrous conditions to form alkyl magnesium halides (R-MgX⁺). Because of the low electronegativity of magnesium, the carbon atom attached to it has a large concentration of negative charge. This negative carbon has a high affinity for hydrogen and is capable of taking it even from very weak proton donors such as water, ethanol, amines or carboxylic acids. These reagents react with the Grignard reagents to evolve the corresponding hydrocarbons.

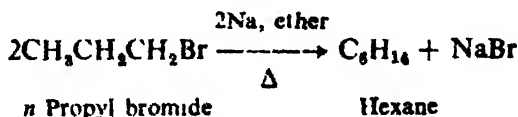


4. *Kolbe's Synthesis:* This method involves the electrolysis of the sod. salt of a carboxylic acid (RCOO⁻Na⁺) to yield an alkane (R-R). The process is regarded as a free radical reaction as shown below:



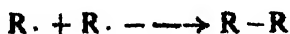
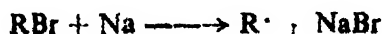
The carboxylate ion loses an electron at the anode to yield the species CH₃COO[·]. This immediately evolves CO₂ to generate a CH₃ radical, which couples to give a hydrocarbon. It is an example of electroorganic synthesis.

5. *Wurtz Reaction:* By heating an alkyl halide with sodium in dry ether, it has been possible to prepare symmetrical hydrocarbons; for instance, hexane can be obtained from propyl bromide and sodium metal.



Mechanism

Two mechanisms have been suggested for this reaction, one involving a free radical as an intermediate and the second is considered to involve sodium

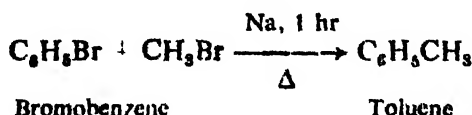


alkyl as an intermediate, which then forms the product in a nucleophilic displacement reaction involving a second alkyl halide molecule.



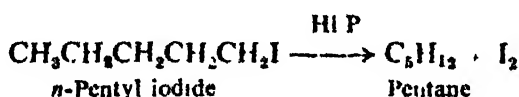


Hydrocarbons with an odd number of carbon atoms cannot be prepared by this method due to the formation of a mixture of hydrocarbons which may be difficult to separate. For the preparation of unsymmetrical hydrocarbons, particularly alkyl hydrocarbons, a modified procedure called the *Wurtz-Fittig* reaction is employed. The procedure consists of heating an aliphatic and an aromatic halide with sodium in an inert atmosphere. It is demonstrated for the preparation of toluene.

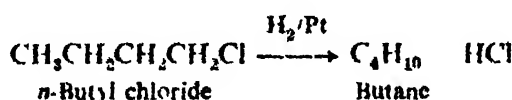


Mixed products are also obtained in this procedure due to the reaction between similar halides, but can be separated on the basis of their physical properties.

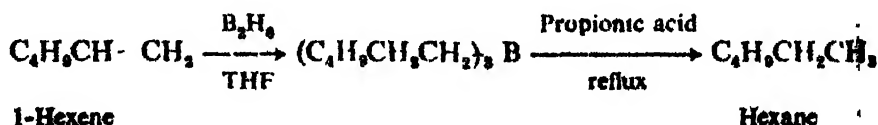
6. *Reduction of Alkyl Halides*: A reducing mixture consisting of hydroiodic acid and red phosphorus converts an alkyl halide to the corresponding hydrocarbon.



7. *Hydrogenolysis*: The carbon-halogen bond can be cleaved in the presence of hydrogen and platinum as catalyst. The process is referred to as *hydrogenolysis*. The result is the formation of a hydrocarbon.



8. *Hydroboration of alkenes*: The usefulness of hydroboration reaction in synthesis arises from the fact that the alkyl boranes can be transformed into a wide variety of products on further reaction. Diborane, for example adds to alkenes to give trialkyl boranes which on refluxing with acid yield hydrocarbons.



7.4 REACTIONS OF ALKANES

The alkane hydrocarbons are inert to many chemical reagents and can undergo reactions under only drastic conditions.

1. **Combustion:** Probably the most important use of paraffin hydrocarbons is as fuels. They burn in excess of oxygen to form carbon dioxide and water. Since a large amount of energy is released, it forms the basis of gasoline as a fuel in engines.

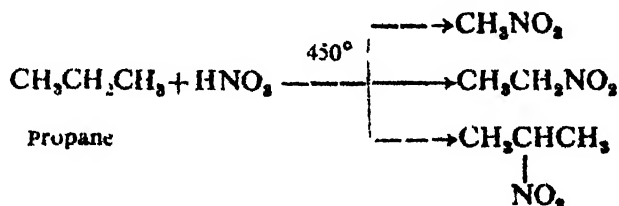


Liquid alkanes such as octane should be vaporized before they will burn.



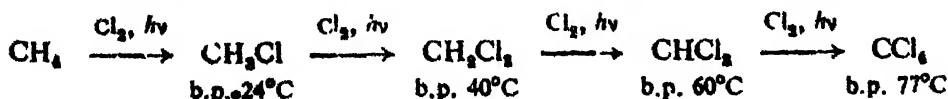
This is the reaction which takes place in the internal combustion engine. However, if the supply of oxygen is inadequate then incomplete combustion occurs and the poisonous gas carbon monoxide is produced. Certain percentage of CO is always present in the exhaust gases of automobiles. Carbon monoxide interferes with the transfer of oxygen in the body by reacting with haemoglobin, the red pigment of the blood.

2. **Nitration:** At high temperatures, alkanes react with nitric acid to form a mixture of nitro-paraffins which find uses in the synthesis of explosives and as solvents.



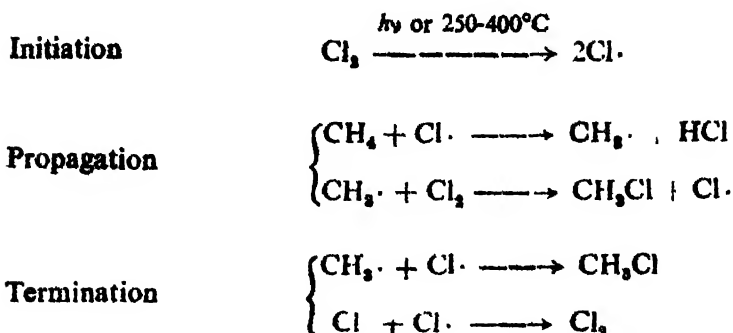
3. **Halogenation:** The halogenation of alkanes can be carried out under controlled conditions and this constitutes an important industrial process for the preparation of halo-alkanes. Halogens like chlorine and bromine do not react easily with alkanes but do so in the presence of either ultra-violet light or at high temperature.

Heating decomposes chlorine molecules into atoms which undergo reaction with alkanes. The final product, for instance, between methane and chlorine is carbon tetrachloride. Mono-substitution with chlorine on methane yields a single monochloro product, it can therefore be inferred that all hydrogens in methane are chemically equivalent. Photochlorination is used industrially for producing a mixture of alkyl halides from petroleum hydrocarbons and



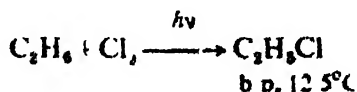
for chlorination of aromatic side chains. The halogens differ in their reactivities, the order being $\text{F}_2 > \text{Cl}_2 > \text{Br}_2 > \text{I}_2$. Fluorine is too reactive to be employed as a halogenating agent while iodine is unreactive.

Mechanism: The reaction proceeds through a free radical chain mechanism.

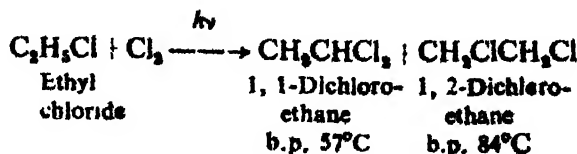


In the initiation step chlorine radicals are produced by breaking the Cl—Cl covalent bond under the influence of heat or light. At temperatures below 100°C , the thermal energy of the mixture cannot break an appreciable number of either the Cl—Cl or the C—H bonds in the reaction mixture. Homolysis of Cl—Cl bond takes place as the temperature is raised. Alternatively, chlorine absorbs light in the 3000 to 6000 Å region (visible) which results in the rupture of the Cl—Cl bond to generate free radicals. The chlorine atoms react rapidly and abstract a hydrogen atom from methane yielding a methyl free radical and hydrogen chloride. This free radical combines with chlorine to form methyl chloride and regenerates a chlorine atom. This chlorine atom is used over and over again in the reaction till all the chlorine molecules are exhausted and the chain is terminated. It is possible that hundreds or even thousands of chain propagation steps may be occurring simultaneously. Chlorination of methane is exothermic by -23 kcal/mole . The termination step involves the combination of different free radicals and thus reduces the yield of the desired product.

Similarly, mono-chlorination of ethane yields only a single product,



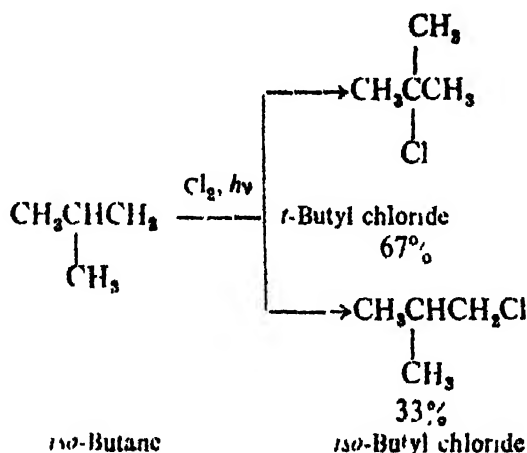
chloro-ethane. However, thermal or photochemical chlorination of chloroethane gives two isomeric products. These are positional isomers. Unlike methane derivatives, the hydrogens of chloroethane are thus



chemically non-equivalent.

An interesting feature of this reaction is that the attack of the chlorine atom on the hydrocarbon is selective, i.e., a tertiary C—H hydrogen atom is abstracted much easier than a secondary or a primary hydrogen. In other words, the rate of abstraction of hydrogen atom follows the order $3^\circ > 2^\circ > 1^\circ$. Thus in the case of isobutane the two products tertiary butyl chloride and isobutyl chloride are formed in a ratio of 2 : 1 even though there are nine primary hydrogen atoms in comparison to only one tertiary hydrogen atom in this molecule.

Therefore, it is likely that the activation energy required to form a tertiary

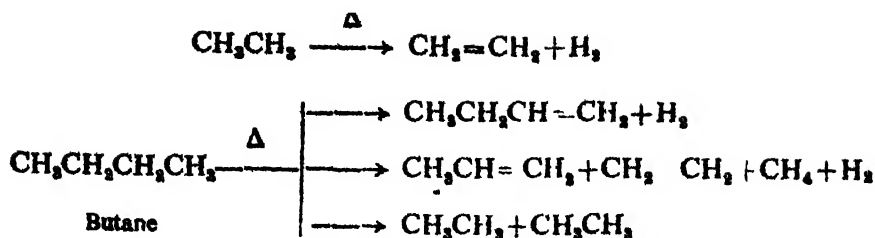


free radical is much less than that for the formation of a primary free radical. The ease of formation of free radicals thus parallels their stability, i.e. $3^\circ > 2^\circ > 1^\circ$. Thus, more stable a free radical, the more easily it is formed. This is depicted on a potential energy diagram (Fig. 7.1)

Bromination of alkanes is rather slow because the activation energy for the first propagation step is almost 15 Kcal/mole higher than in chlorination. But at the same time bromine is more selective in its attack. It attacks a tertiary carbon atom predominantly. This is evident from the fact that in contrast to chlorination, bromine reacts with *iso*-butane to give 99% of *tert* butyl bromide

Bromine is less reactive, iodine reacts still slower because the activation energy for the first propagation step is much higher (about 33 Kcal/mole).

4. *Cracking (Pyrolysis)*: At high temperatures, the paraffin hydrocarbons cleave into smaller fragments. Methane is the most stable hydrocarbon because of a higher C—H bond energy (98 kcal/mole), but the higher paraffins are thermally less stable. Ethane decomposes to ethylene at 600-800°, but butane fragments do so at 400-600°.



The petroleum industry uses pyrolysis to convert higher into smaller hydrocarbons which are useful as fuels. This type of reaction is called *cracking*.

5. *Isomerization*: As stated earlier, branched chain hydrocarbons have excellent antiknock properties. Therefore, conversion of a straight chain to a branched chain hydrocarbon is a desirable process. This is accomplished in the presence of a Lewis acid catalyst, AlCl_3 .

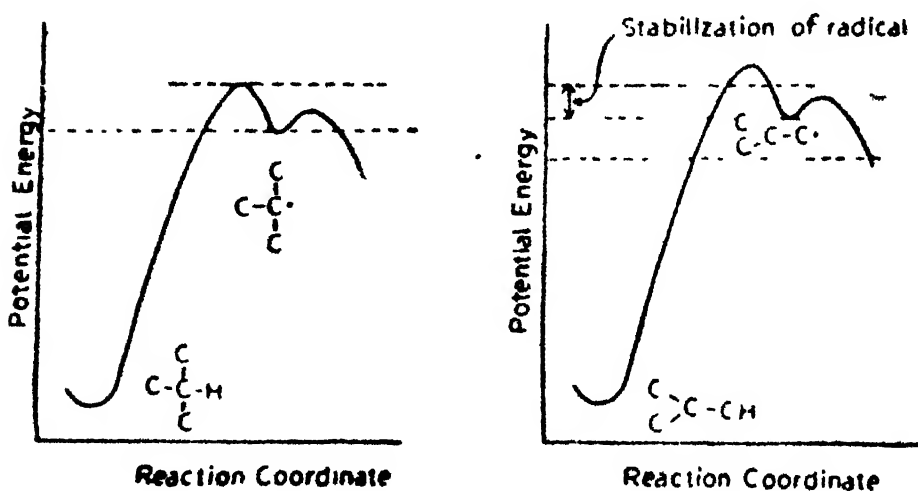
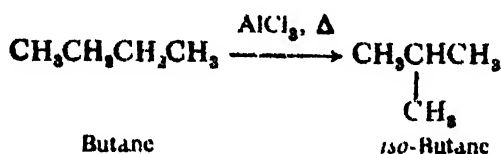
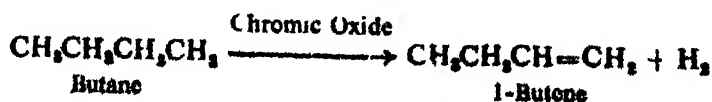
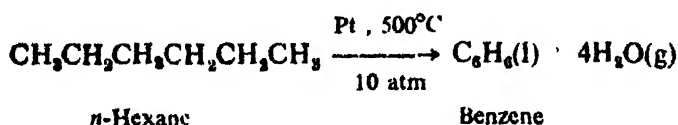


Fig. 7.1 Stability of tertiary and primary free radicals

6. *Catalytic Dehydrogenation*: When alkane vapors are passed over chromic oxide catalyst, it loses two hydrogen atoms, i.e., it is dehydrogenated to an unsaturated compound.



7. **Aromatization (Reforming):** Alkanes on heating in the presence of a platinum catalyst produce aromatic compounds. A large number of important chemicals are derived from petroleum, one of them is benzene.



7.4.1 Uses of Alkanes

Alkanes are used as raw materials for making explosives, in the rubber industry, in synthesizing organic chemicals and as solvents.

7.5 PHOTOCHEMICAL REACTIONS

Thermal reactions are promoted by heat whereas a photochemical reaction derives its energy from the absorption of light radiation. A *photochemical reaction* is thus any reaction initiated by ultraviolet or visible light. In nature, *photosynthesis* is a familiar photochemical reaction.

The absorption or emission of radiation by a molecule is a quantized process, i.e., a molecule absorbs light energy in terms of quantum, and the magnitude of energy (E) absorbed is given by the following equation:

$$\Delta E := h\nu = hc/\lambda$$

where ν represents the frequency of the incident light, c is the velocity of light, λ is the wavelength and h is the Planck's constant. Thus light of 300 nm wavelength has an energy equal to 95 kcal/mole. This is the amount of energy of most C—C single bonds and is enough to bring about a chemical reaction. All covalently bonded carbon compounds, however, do not absorb light, while others are converted to stable excited states. For a reaction to take place, a molecule must absorb energy in the wavelength region in which it is irradiated. This can be determined from the absorption spectrum of the molecule.

Photochemical reactions are largely those of π -electron systems in which case the molecule absorbs a photon and one bonding π -electron is excited to an anti-bonding orbital, i.e. π^* . This is also known as π - π^* transition. Most organic molecules have an even number of electrons and are paired. In each pair, the opposing electron spin cancel and the molecule possesses no resultant spin such an electronic state is referred to as *singlet*. Most of the organic molecules in the ground state are in singlet state. When a molecule absorbs light, it is excited to a singlet state (S_1) of the molecule. This state is short lived. In this state, the molecule has a number of paths open to it. It may return to the ground state by emission of a photon, it may transfer its energy to another molecule (sensitization) it may cross-over to the triplet

state (inter-system crossing) or it may undergo chemical reactions such as decomposition, isomerization or rearrangements.

A *triplet state* is described as one in which the spin of the two electrons is not paired. The majority of the photochemical reactions takes place via a longer lived triplet state (T_1). The subject of photochemistry has been expanding very rapidly and photochemical reactions find extensive applications in organic syntheses and in the preparation of agricultural and industrial chemicals.

7.6 PETROLEUM

Petroleum (Latin *petra*-rock; *oleum*-oil) is a dark colored viscous liquid as it is obtained from oil wells. It is a complex mixture of hydrocarbons, principally alkanes and cycloalkanes. Organic compounds containing N, S, O, etc., are also present in varying proportions. Petroleum is a source of fuels and raw materials for the chemical industry. Extensive exploration of oil fields and the development of the photochemical industry has attracted the attention of the world in the last two decades.

7.6.1 Occurrence

Petroleum occurs deep down the earth as a black viscous oil. The surface of the oil is covered with the volatile hydrocarbons, the *natural gas*. The main oil producing countries in the world are: Russia, United States of America, Nigeria, Venezuela, Iran, Iraq, Saudi Arabia and other countries in the middle east. The world output of oil is more than one billion tons annually. Its use fulfills nearly 50% of the energy requirement for the entire world. The Persian gulf states have about 56% of the world's oil resources. Among these, Saudi Arabia has world's largest oil fields. India has to import crude petroleum to meet its increasing needs. Recently, however, oil fields have been discovered offshore Bombay and that region is known as Bombay High. It produces more than a million tons of crude every month and has thus saved crores in foreign exchange. The ageing Gujarat oil fields have been giving a diminishing yield. Therefore, another viable area that is being explored is the Assam-Arakan basin lying deep in the jungles and mountain terrain, to meet the deficit. The refining work is handled principally by various companies such as Hindustan Petroleum (formerly ESSO); Bharat Petroleum Company (formerly Burmah Shell); Assam oil and Indian Oil Corporation. Major refineries are located at Barauni (Bihar), Bangaigaon (Lower Assam), Haldia (West Bengal), Mathura (U.P.), Cochin (Kerala), Digboi (Assam) etc. and one is being built in Karnal (Haryana).

7.6.2 Composition

The composition of petroleum varies from field to field. In general, it contains varying proportions of paraffins, naphthenes and aromatic hydrocarbons. Small amounts of unsaturated hydrocarbons containing S, N and

O, in addition to C and H are also present. The various constituents may be listed as follows:

1. *Lower Paraffins*: Paraffin hydrocarbons containing upto six carbon atoms.
2. *Higher Paraffins*: Straight chain hydrocarbons upto decane and branched chain hydrocarbons from *iso*-butane to methylnonanes.
3. *Cyclo-Paraffins*: Several alkyl derivatives of cyclopentane and cyclo-hexane have been isolated. In petroleum chemistry, these compounds are known as *naphthenes*.
4. *Aromatic Hydrocarbons*: Benzene, toluene, xylene, cumene and many other aromatic compounds are present in petroleum.
6. *Sulfur and Nitrogen Compounds*: Heterocyclics containing sulfur and nitrogen are also present.
6. *Oxygen Compounds*: The principal oxygen compound present is a carboxylic acid known as naphthenic acid.

7.6.3 Origin

Petroleum is the product of ages of geological synthesis. Several theories have been advanced to account for the origin of petroleum. Among these two of them are the following:

7.6.3(a) Engler's Theory

This theory maintains that petroleum derives its origin from animal and marine life, which under high pressure and temperature, decomposed to form petroleum.

7.6.3(b) Modern Theory

Presently, it is believed that petroleum is the result of decomposition, under anaerobic conditions, of vegetable organism which had been buried under the earth's crust for long periods of time. The initial stage of putrefaction may have been biochemical, followed by a complete oxidation of this material under moderately high pressures and temperatures causing its conversion to petroleum, and this collected in pockets as a black liquid. The mechanism of the conversion of primary organic matter into petroleum hydrocarbons is not known.

7.6.4 Refining

Petroleum is obtained by drilling wells to get it out of the earth. The crude oil is transported to the refineries by pipelines or tankers. Refining, in the case of petroleum, includes any process applied to the crude oil to separate it into different components. The first stage in the refining of petroleum is fractional distillation, whereby lighter and heavier portions are separated. The important fractions so obtained are listed below:

Fraction	Boiling Range (°C)	Composition	Uses
Natural gas	Below 20	C ₁ -C ₄	Fuel in gas cookers and domestic heating
Petroleum ether	20-60	C ₅ -C ₆	Solvent in industry
Ligroin or light naphtha	60-90	C ₇	Solvent and in dry cleaning
Straight chain gasoline	85-200	C ₈ -C ₁₂	Fuel in diesel engine, cars, etc
Kerosene	200-300	C ₁₂ -C ₁₅	Fuel
Heating fuel Oil	300-400	C ₁₅ -C ₁₈	Heating fuel
Lubricating oil	400	C ₁₈ -C ₂₄	Lubrication
Paraffin	Solid	C ₂₅ -C ₄₀	Ointments, candles and polishes
Asphalt (Bitumin)	Residue	> C ₃₀	Fuel in the steel industry and for tarring roads

Crude oil has a broad boiling range. The low boiling constituents, namely propane, butane, etc., are gases at ordinary temperatures. These are removed by a process known as *scrubbing*. This involves the dissolution of these substances into a high boiling liquid and then separation by distillation. *Light petroleum ether* consists mainly of pentanes and hexanes. Ligroin is a mixture of heptanes with the boiling range from 60-90°. Kerosene is a mixture of hydrocarbons and is the most important petroleum fraction (200-300°C) which is employed as a fuel. Because of the numerous uses of gasoline and its small proportion in the distillate, kerosene and fuel oil fractions (i.e. high boiling fractions) are converted to gasoline to augment its yield by a process called *cracking*. This process converts larger hydrocarbons into smaller hydrocarbons and this can be accomplished by different methods. The catalytic process nowadays is favored over the thermal process, because a proper selection of catalyst enables the desirable products to be obtained in large quantities. Moreover, it can be effected at low temperatures. The gasoline produced by catalytic cracking has a high octane number, i.e., it has got good antiknock properties.

Petrochemicals are chemicals made from petroleum or natural gas. The hydrocarbons containing six carbon atom or less are the starting materials for the manufacture of a large number of petrochemical products, such as plastics, fibres, polyesters, nylon, dyes, rubber, pharmaceuticals, insecticides, etc.

7.7 FUELS, KNOCK AND OCTANE NUMBER

During the combustion of petrol vapors inside an automobile cylinder, a large quantity of hot gases is produced. The gases force the piston down the cylinder and the power generated is transmitted to the wheels. For smooth running of the engine, the ignition of gasoline and oxygen should take place when the piston is at the right point in the cylinder. To obtain maximum energy the mixture of gasoline and oxygen is compressed, this compression can result in self-ignition. In other words, the ignition of gases takes place before the spark. This causes sudden rise in pressure which delivers a blow to the piston. The engine makes a noise called "*Knocking*." This wastes fuels and reduces the life of the engine. It is thus desirable that a fuel has *anti-knocking* characteristics. It is known that the knocking characteristics are associated with the structure of the constituents of the fuel. In order to compare the performance of various gasolines it was necessary to develop a knock rating which is termed as the *octane number*. It is a numerical rating that indicates how well a gasoline resists combustion knock. For this purpose a single alkane known to be the best fuel for resistance to knocking was chosen and *iso*-octane (2, 2, 4-trimethylpentane) was such an alkane, and was arbitrarily assigned the octane number of 100. The straight chain *n*-heptane was given the octane number of zero because it has poor anti-knocking property. The *octane number* of a fuel is thus described as the percent by volume of *iso*-octane that must be blended with *n*-heptane to produce a blend having the same *anti* knocking characteristics as the gasoline under study. The octane number of a gasoline is determined by comparing its performance in engine tests with the performance of a mixture of *iso*-octane and *n*-octane. The proportions of the mixture are varied until the mixture produces a knock of the same intensity as that produced by gasoline. If equality of proportion occurs when the mixture is 80% *iso*-octane, and 20% of heptane, for example, then the gasoline has an octane number of 80. Among the paraffins and olefins, the octane number decreases as the chain length increases, but this number is higher for compact molecules. This is illustrated by the following examples:

<i>n</i> -pentane	61
2, 2-dimethylpentane	83
2, 3-dimethylbutane	95
2, 3, 3-trimethylpentane	99
2, 2, 4-trimethylpentane	100

Cetane number: It is a measure of the ignition quality of the diesel fuel and is analogous to the octane rating of gasoline. The cetane number is measured by comparing the ignition delay of the test fuel with that of fuels

containing different percentages of cetane and α -methylnaphthalene. Cetane has a short delay period while α -methylnaphthalene ignites slowly. The cetane composition of the reference fuel and the test fuel have equal ignition delay period. The cetane number of the test fuel is thus equal to the percentage by volume of cetane in the reference fuel at this point. For medium and high speed engines the cetane number should be between 40 and 60.

The quality of a fuel can be improved by the addition of certain compounds known as *anti knocking agents*, such as tetraethyl lead $(C_2H_5)_4Pb$. The function of such compounds is to convert a gasoline into branched hydrocarbons by alkylation and polymerization.

7.8 SYNTHETIC GASOLINE (FUELS)

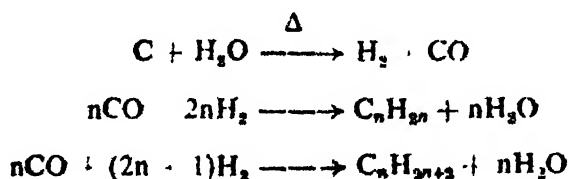
Because of the increasing demand of gasoline, it is also obtained synthetically from coal. Two methods were developed at the time of World War II in Germany.

7.8.1 Bergius Process

Coal is a mixture of hydrocarbons and can be heated in the presence of hydrogen at $450-480^\circ$ and at a pressure of 200 atmospheres. A catalyst, 5% iron oxide, is also employed. The mixture is then fractionally distilled to obtain a high quality gasoline (octane number 75-80)

7.8.2 Fischer-Tropsch Process

It consists of the hydrogenation of water gas produced by the action of steam on red-hot coke.

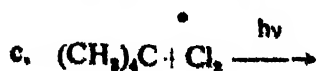
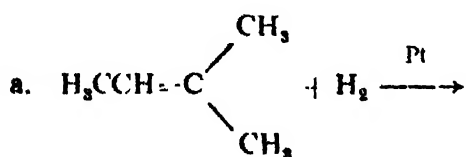


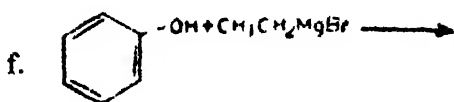
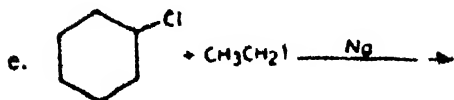
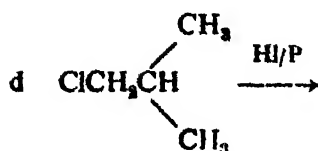
Carbon monoxide and hydrogen gas are passed over an iron oxide catalyst and the mixture is heated at $200-300^\circ$. It is then fractionally distilled. The motor fuel so obtained has a low octane number (40), further processing is thus needed to obtain a premium fuel.

The world's demand for fuel nowadays is astronomical. This has led to a considerable depletion of the natural sources. As a result, mankind faces a severe energy crisis. Additional sources of energy such as solar, nuclear and hydroelectric are being intensively developed. Other potential sources of energy are the vegetable and animal wastes. Methods for the production of petroleum are being looked into. Recently *Gobar Gas* plants have been set in our country to produce gas for heating, cooking and industrial purposes.

QUESTIONS

- 7.1 What is cracking? How is it useful in the petroleum industry?
- 7.2 Write structures for all the isomers of the formula C_4H_{10} .
- 7.3 Write structural formulas for the following compounds:
- 3,3-Dimethyl-4-ethylhexane
 - 2,2-Dichloro-3-bromo-3-methylheptane
 - neo*-Pentane
 - iso*-Butane
 - 2-Cyclobutyl-3,3-dimethylheptane
 - iso*-Octane
 - 4-(1-Ethylpropyl)-2-methylnonane
 - 4-isopropyl-3-methylheptane
- 7.4 Which of the isomeric pentanes can form only one mono-chloro substitution product?
- 7.5 What is meant by the term octane number? Also what does it mean by a certain gasoline having an octane rating of 85.
- 7.6 Give reasons for the following:
- Octane has a m.p. -57° while 2,2,3,3-tetramethylbutane 101° .
 - A tertiary free radical is more easily formed than a primary free radical.
 - Ethanol is soluble in water but ethane is not.
 - Methane is more stable than other higher alkanes.
 - The quality of a fuel is improved by the addition of tetraethyl lead.
- 7.7 Describe the mechanism for the formation of benzyl chloride from toluene by photochlorination.
- 7.8 Write the products of each of the following reaction:





7.9 Write a short note on the photochemical reactions

7.10 A sample of gaseous hydrocarbon occupying 1.2 litres at N.T.P. when completely burnt in air produced 2.2 g of CO_2 and 1.8 g of H_2O . Calculate the weight of the compound taken and the volume of oxygen at N.T.P., required for its burning. Find the molecular formula of the hydrocarbon.

- 7.11 a. What are the theories regarding the origin of petroleum?
 b. What is meant by cracking in the petroleum industry?
 c. State any one method for the synthesis of petrol.

- 7.12 a. Discuss the reactivity of halogens towards methane
 b. Write a note on the combustion of alkanes

7.13 A mixture of ethyl- and isopropyl-iodides is heated with metallic sodium in dry ether. Predict the products

7.14 Describe briefly what is meant by the following terms:

Reforming, knocking, octane number, petrochemicals and scrubbing.

7.15 Indicate with relevant equations three different methods for the conversion of *iso* butyl bromide to *iso*-butane.

7.16 Write the possible mono-substitution products that would be obtained by the chlorination of isopentane at 300°C , which isomer would you expect to predominate?

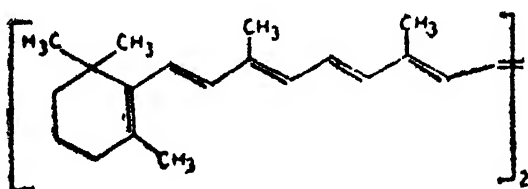
7.17 Discuss the selectivity in the chlorination and bromination of *iso*-butane.

7.18 Explain why branched alkanes have lower boiling points than the corresponding straight chain isomers.

8

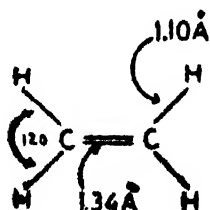
Alkenes or Olefins

The class of organic compounds that contains a $C = C$ bond is called *alkenes* or *olefins*. They have two hydrogen atoms less than the corresponding alkanes and are obtained during the cracking of alkanes. The carbon-carbon double bond is sometimes called an *-ene* function and it occurs widely in nature from substances in petroleum to fats and oils to vitamins and hormones. Compounds containing several double bonds are of particular significance in biochemistry, for instance, β -Carotene, the yellow coloring matter is present in many plants such as carrots and tomatoes.

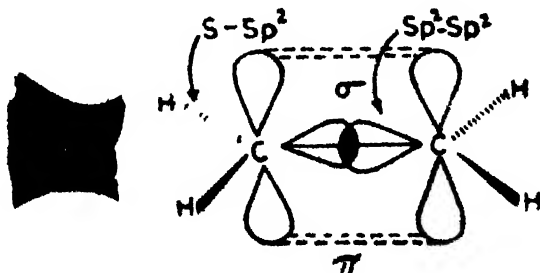


β -Carotene

Compounds with two double bonds are called dienes. Alkenes possess the general molecular formula C_nH_{2n} . Methylene, CH_2 , which should have been the first member of the homologous series does not exist in the stable form. The series, therefore, commences with ethylene and its structure is given below:



Structural Formula
of Ethylene



Molecular Orbital Representation
of Ethylene

The C—C bond formed by lateral overlap of two carbon sp^3 hybrid orbitals has an internuclear distance of 1.34 \AA which is shorter than the normal C—C distance (1.54 \AA) because the carbon atoms are held more tightly in ethylene. The C—C bond, is composed of a σ and a π bond; the latter is the distinguishing feature of an alkene and is responsible for its chemical reactivity. The unhybridized $2p_z$ orbitals on each carbon atom, that are perpendicular to the plane of sp^2 orbitals, overlap by a new kind of overlap, i.e. the side-side overlap to form the π -bond. The lobes extend both

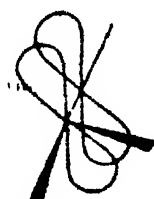


Fig. 8.1

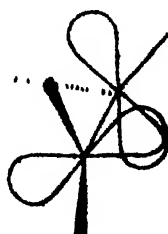
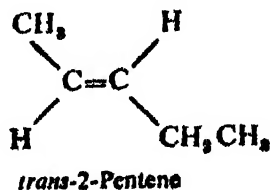
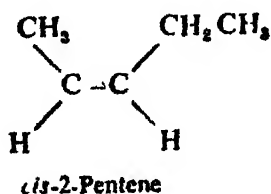


Fig. 8.2

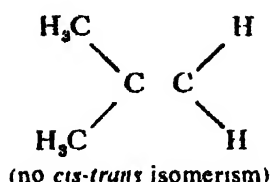
above and below the plane of the sp^2 orbitals. The p -orbitals overlap is maximum when such orbitals are parallel to each other, (Fig. 8.1) but perpendicular and a strong bond results. If the orbitals are not parallel (Fig. 8.2), then a weaker bond results because of insufficient overlap. Ethylene is planar and the bonds subtend an angle close to 120° which is the angle at which each of the three groups attached to the olefinic carbon atoms are farthest apart. The π -bond is also present in the carbonyl group

$\left(\begin{array}{c} \diagup \\ \text{C} - \text{O} \\ \diagdown \end{array} \right)$ in which the carbon and oxygen atoms are linked together by a double bond. Restricted rotation about the C=C bond in alkenes gives rise to geometric isomerism. This is illustrated by the following example.



In the *cis*-isomer, similar or bulky groups are on the same side of the double bond while on opposite side in the *trans*-isomer. If one of the carbon atoms, of the double bond is linked to two similar groups than

cis trans isomerism is not possible. The alkene, 2-methyl-1-propene has no *cis-trans* isomers.

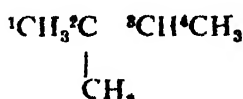


8.1 NOMENCLATURE OF ALKENES

The rules stated in Sec. 2.3 apply in the naming of alkenes; the suffix *-ane* for alkanes is changed to *-ene*, i.e. an alkene. The position of the double bond along the chain is indicated by a number and both doubly bonded carbon atoms are given the lowest possible numbers.

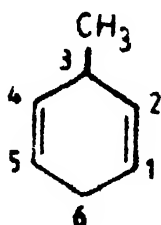
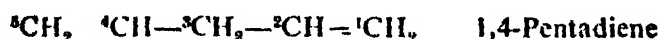


1-Butene
(But-1-ene)



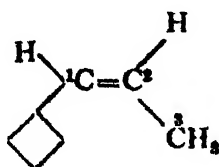
2-Methyl-2-butene
(2-Methylbut-2-ene)

If the suffix starts with a consonant then the letter *a* is also attached as is evident from the following, the suffix is diene if two double bonds are present.



3-Methylcyclohexa-1, 4-diene

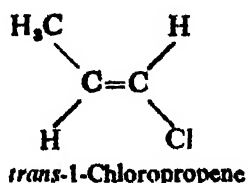
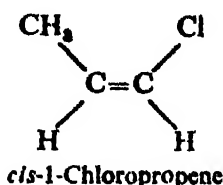
If necessary, a prefix *cis* or *trans* is employed, for geometric isomers.



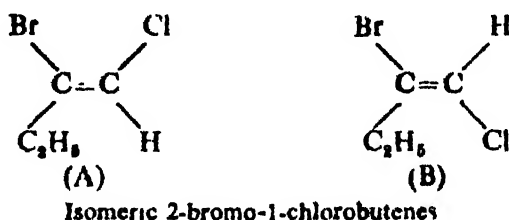
cis-1-Cyclobutyl-1-propene

8.1.1 The E-Z Nomenclature for Alkenes

An additional example may be described for *cis*- and *trans*-1-chloropropenes.



The *cis-trans* nomenclature of alkenes is convenient in simple cases as shown above. Many geometric isomers, however, that have more than two atoms or groups of atoms other than hydrogen bonded to the olefinic carbon atoms cannot be named by the *cis-trans* system of nomenclature. For instance, isomeric 2-bromo-1-chlorobutenes have three different groups bonded to the carbon-carbon double bond. On the basis of the *cis-trans* nomenclature, either of these can be named as *trans*-2-bromo-1-chlorobutene



because in structure (A) chlorine is *trans* to ethyl while in (B) chlorine is *trans* to bromine. This can thus lead to confusion in naming such isomers. The chemical abstracts service has proposed an unambiguous system that has been adopted by the IUPAC. This is termed the *E-Z system of nomenclature*. According to this system, the two groups attached to each end of the carbon-carbon double bond are assigned priority numbers in the same way as enantiomers by *R/S* configuration using the *Cahn-Ingold-Prelog (CIP) sequence rules*. When the groups of higher priority on adjacent carbons are on opposite side, configuration is *E* (from the German Word, entgegen, opposite). If the groups of higher priority are on the same side, the configuration is *Z* (from the German word, zusammen, together). Four sequence rules are used to determine priorities. These rules were discussed in connection with *R/S* configuration (see Chapter 4)

8.2 PHYSICAL PROPERTIES OF ALKENES

The alkenes possess physical properties similar to the saturated hydrocarbons, the alkanes. The melting points of highly substituted alkenes are higher compared to the straight chain olefins. Their boiling points increase gradually, as is clear from Table 8.1, by 20–30° per carbon atom, as the carbon chain increases in length. They are insoluble in water or ethanol but soluble in non-polar solvents namely ether, benzene or ligroin. Like

alkanes, the alkenes are also non-polar. Alkenes show geometric isomerism and the *cis* form possess a dipole moment (Table 8.2) while the *trans*-alkenes do not. Furthermore, a *trans*-isomer is usually more stable than the *cis*-isomer because of the steric interactions of the bulky groups in the latter at both the olefinic carbon atoms. The alkenes do not display optical isomerism.

Table 8.1. Physical Properties of Alkenes

Hydrocarbon	Structure	Melting Point (°C)	Boiling Point (°C)	Density
Ethylene	$\text{H}_2\text{C}=\text{CH}_2$	-169	-102	
Propylene	$\text{H}_2\text{C}=\text{CHCH}_3$	-185	-48	0.5193
1-Butene	$\text{H}_2\text{C}=\text{CHCH}_2\text{CH}_3$		-6.5	0.5951
1-Pentene	$\text{H}_2\text{C}=\text{CHCH}_2\text{CH}_2\text{CH}_3$		30	0.6405
1-Hexene	$\text{H}_2\text{C}=\text{CHCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$	-138	63.5	
<i>cis</i> -2-Butene	$\begin{array}{c} \text{H}_3\text{C} \quad \quad \text{CH}_3 \\ \quad \backslash \quad / \\ \quad \text{C} = \text{C} \\ \quad / \quad \backslash \\ \text{H} \quad \quad \text{H} \end{array}$	-139	4	0.6213
<i>trans</i> -2-Butene	$\begin{array}{c} \text{CH}_3 \quad \quad \text{H} \\ \quad \backslash \quad / \\ \quad \text{C} = \text{C} \\ \quad / \quad \backslash \\ \text{H} \quad \quad \text{CH}_3 \end{array}$	-106	1	0.6042
<i>iso</i> -Butylene	$\begin{array}{c} \text{CH}_3 \\ \quad \backslash \\ \quad \text{C} = \text{CH}_2 \\ \quad / \\ \text{CH}_3 \end{array}$	-141	7	
<i>cis</i> -2-Pentene	$\begin{array}{c} \text{CH}_3 \quad \quad \text{CH}_2\text{CH}_3 \\ \quad \backslash \quad / \\ \quad \text{C} = \text{C} \\ \quad / \quad \backslash \\ \text{H} \quad \quad \text{H} \end{array}$	-151	37	0.6556
<i>trans</i> -2-Pentene	$\begin{array}{c} \text{CH}_3 \quad \quad \text{H} \\ \quad \backslash \quad / \\ \quad \text{C} = \text{C} \\ \quad / \quad \backslash \\ \text{H} \quad \quad \text{CH}_2\text{CH}_3 \end{array}$		36	0.6482

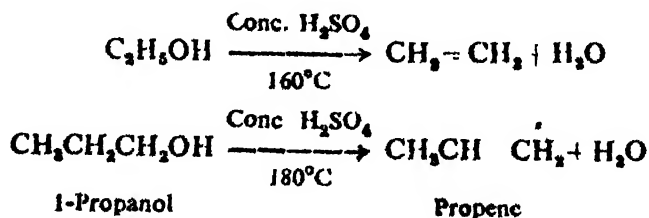
Table 8.2 Dipole Moments of Alkenes

Hydrocarbon	Structure	m.p. (°C)	b.p. (°C)	Dipole Moment (μ l)
<i>cis</i> -2-Butene	$ \begin{array}{ccc} \text{CH}_3 & & \text{CH}_3 \\ & \diagdown & / \\ & \text{C}=\text{C} & \\ & / & \diagdown \\ \text{H} & & \text{H} \end{array} $	-139	4	0.33
<i>trans</i> -2-Butene	$ \begin{array}{ccc} \text{CH}_3 & & \text{H} \\ & \diagdown & / \\ & \text{C}=\text{C} & \\ & / & \diagdown \\ \text{H} & & \text{CH}_3 \end{array} $	-106	1	0
<i>cis</i> -1, 2-Dichloro-ethylene	$ \begin{array}{ccc} \text{Cl} & & \text{Cl} \\ & \diagdown & / \\ & \text{C}=\text{C} & \\ & / & \diagdown \\ \text{H} & & \text{H} \end{array} $	-80	60	1.85
<i>trans</i> -1, 2-Dichloro-ethylene	$ \begin{array}{ccc} \text{Cl} & & \text{H} \\ & \diagdown & / \\ & \text{C}=\text{C} & \\ & / & \diagdown \\ \text{H} & & \text{Cl} \end{array} $	-50	48	0

8.3 PREPARATION OF ALKENES

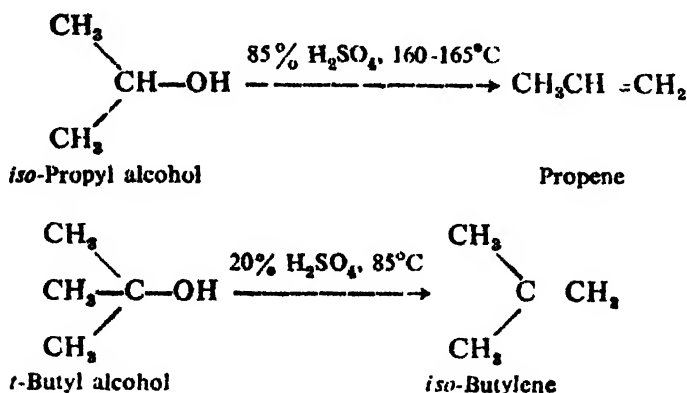
Alkenes are obtained in the petroleum industry by the process of cracking. They can be obtained by several synthetic methods and most of them involve the process of elimination.

1 *Dehydration of Alcohols.* On heating a primary alcohol with concentrated sulfuric acid or phosphoric acid at 180° , an alkene is formed. Propanol, for instance, yields propene under these conditions. Ethylene can be prepared in the laboratory by heating ethanol with conc. sulfuric acid at 160°C .



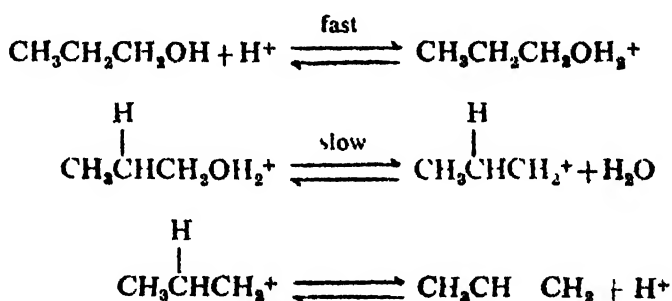
If the temperature is kept at 140° , then an ether results. Secondary and

tertiary alcohols can be dehydrated readily in the presence of dil. sulfuric acid at low temperatures. The ease of dehydration among alcohols is $3^\circ > 2^\circ > 1^\circ$.



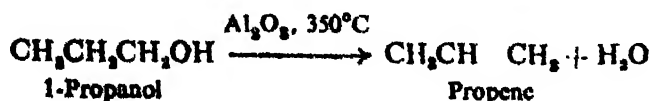
Mechanism

The generally accepted mechanism of dehydration involves the following steps:



The hydroxyl group of alcohol is protonated to form an *oxonium ion*. Then a water molecule is lost to yield a carbocation which rapidly loses a proton to form the alkene. This is an example of an E_1 reaction, i.e. in which only one molecule is involved and is a first order elimination reaction. The order of dehydration is dependent on the stability and ease of formation of the carbonium ion. Since an alkyl group is electron-donating and a tertiary carbonium ion contains three of them, as a result, it is more rapidly formed and thus accounts for the ease of dehydration of tertiary alcohols. Among protonic acids used as catalyst, sulfuric acid is the most suitable because its anion (HSO_4^-), is easily split off from the positive carbon atom as compared to the anions of other acids like HCl.

Water can also be removed from alcohols in the vapor phase in the presence of aluminum oxide, Al_2O_3 , which acts as a Lewis acid.

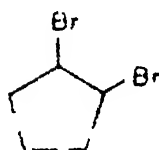
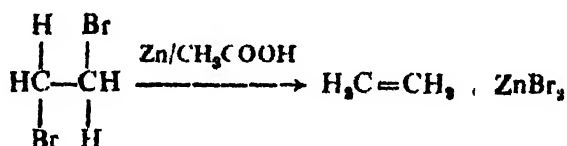


2. *Dehydrohalogenation of Alkyl Halides:* Alkenes can be prepared by heating an alkyl halide in the presence of an alcoholic solution of a base. A molecule of hydrogen halide is lost and the process is known as *dehydrohalogenation*. To favor elimination, a high temperature is employed.

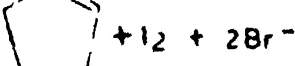
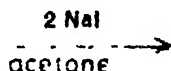


This is an example of an E_2 reaction as it follows second order kinetics.

3. *Dehydrohalogenation of Vicinal Halides:* Vicinal or *vic* halides are dihalo compounds in which halogens are situated on adjacent carbon atoms. The name *geminal (gem)* dihalides is used for those dihalides in which both the halogens are attached to the same carbon atom. Elimination of such compounds takes place under mild conditions in the presence of zinc dust or iodide ion.



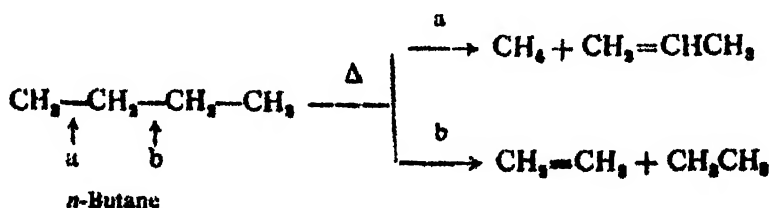
1, 2-Dibromocyclopentane



Cyclopentene

Debromination by zinc takes place on the surface of the metal and the mechanism is uncertain. With NaI , the reaction takes place by L_2 elimination. This reaction, however, is not of much practical utility because dihalides themselves are prepared by the addition of halogen to an alkene.

4 *Cracking:* Petroleum is a complex mixture of hydrocarbons. Heating (above 500°C) of petroleum produces large quantities of a mixture of olefins.

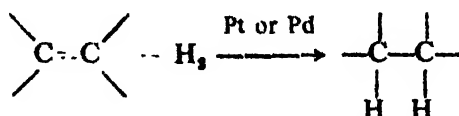


8.4 REACTIONS OF ALKENES

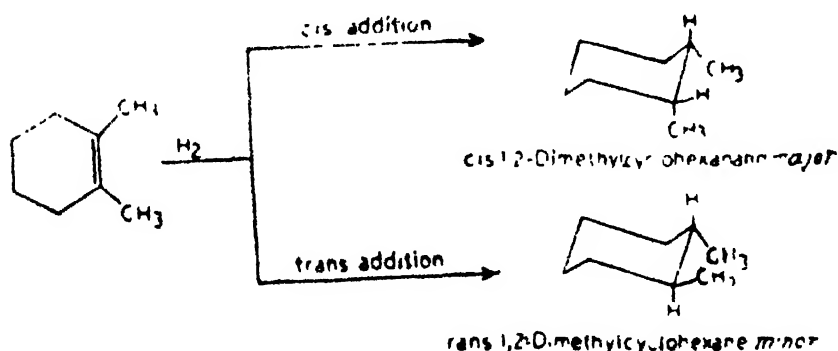
The double bond is the functional group of alkenes and it undergoes a variety of interesting chemical reactions. The most important of these is

the addition to $C=C$ bond to form saturated products. Since olefins are electron rich they are easily attacked by electrophilic reagents.

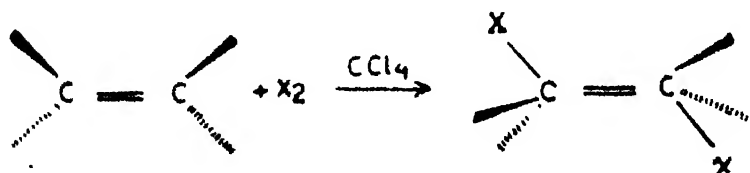
1. *Addition of Hydrogen:* An alkene absorbs hydrogen in the presence of a catalyst, platinum or palladium, at room temperature. Hydrogenation is an exothermic process ($\Delta H^\circ \approx 30$ kcal/mole). Both the hydrogen atoms attack from the same side of the double bond and the process is known as *cis-addition*.



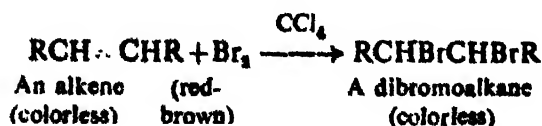
Hydrogenation of 1,2-dimethylcyclohexene leads only to the *cis* product, and the *trans*-isomer is not formed.



2. *Addition of Halogens:* Addition of halogens to alkenes affords vicinal halides, and is a general reaction for their preparation.



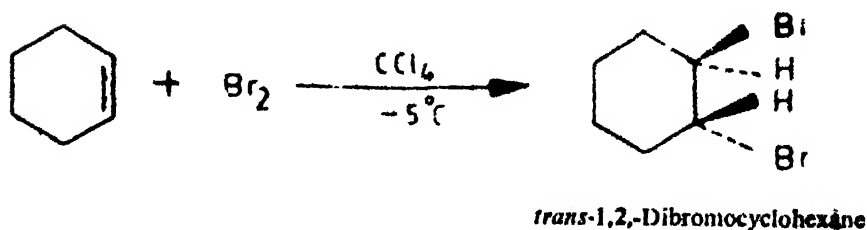
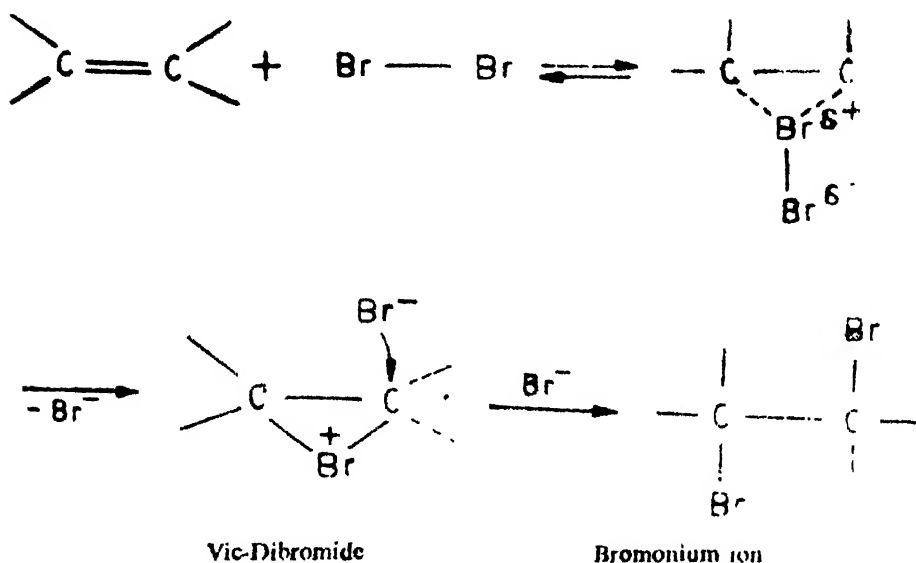
where $X = Cl_2$ or Br_2 .



The addition of bromine to an alkene is used as a qualitative test to detect the presence of unsaturation in a compound.

Mechanism

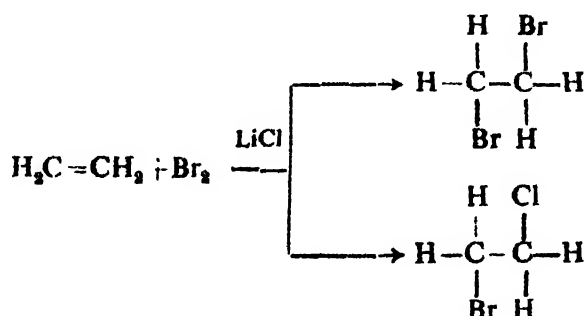
Halogens add in a stepwise polar mechanism. Addition of bromine to alkenes takes place in a stereospecific *trans* manner in contrast to hydrogenation. In the first step bromine molecule is polarized (dipole-induced dipole) in the presence of the C=C bond which is a region of high negative charge density and the positive-end is attached to the double bond to form a cyclic three membered *bromonium ion* intermediate. In the second step, the bromide ion approaches from the opposite side as shown, to form a *trans* product.



A specific example is the addition of bromine to cyclohexene.

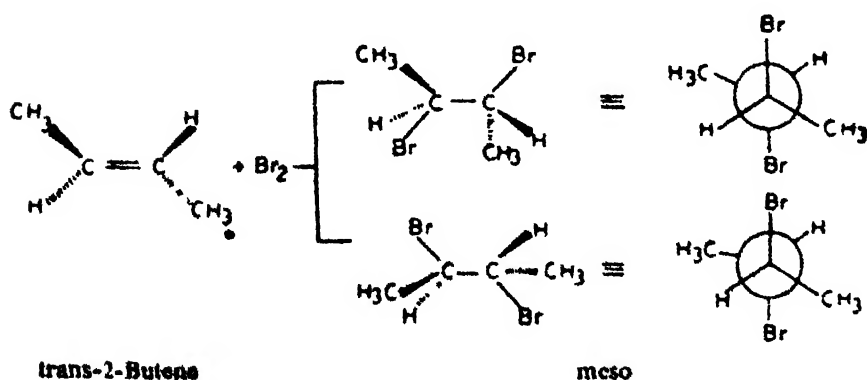
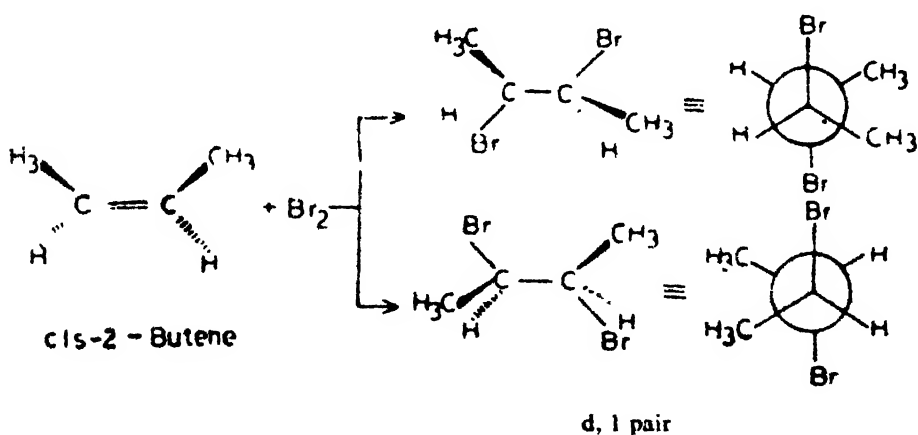
It is noticed that the reaction takes place in two steps. The first step involves the formation of a bromonium ion in the manner shown. In the second step, this ion being a highly reactive species quickly combines with the bromide ion to lead to the product. To prove this, it should be possible to trap the cyclic bromonium ion by adding a different negative ion. This

indeed has been found by adding bromine to alkene in the presence of LiCl. The reaction products were identified as a mixture of 1,2-dibromoethane and 1-bromo-2-chloroethane but no 1,2-dichloroethane because the chloride



ion competes with the bromide ion only after the bromonium ion intermediate has been formed. A fraction of the product is also formed containing an —OH group, by reaction of the intermediate with water used as solvent.

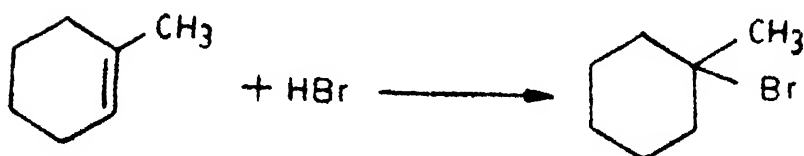
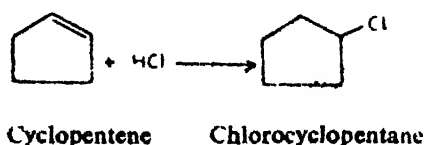
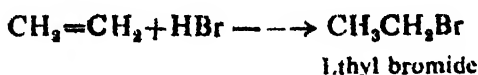
Further evidence that addition is *trans* can be obtained by the bromination of substituted alkenes such as *cis*- and *trans*-2-butenes which yield stereochemically different products.



Addition of bromine to *cis*-2-butene leads to an enantiomeric pair while a *meso* product is obtained from addition to the *trans*-2-butene isomer.

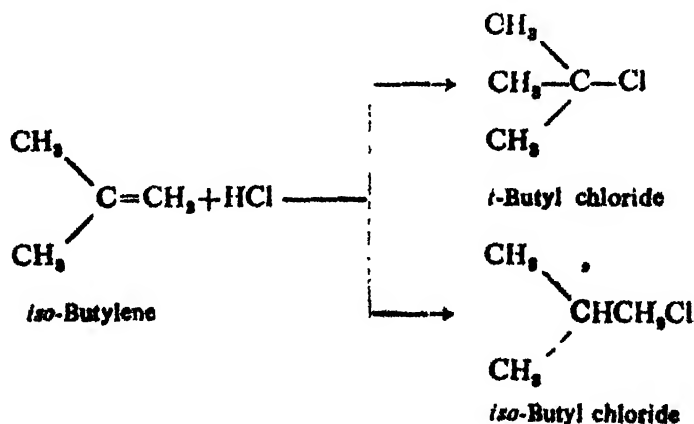
Addition of chlorine to a double bond is less stereospecific. Iodine is added under photochemical conditions.

4. **Addition of Hydrogen Halides:** An alkene is converted into the corresponding alkyl halide by the addition of a hydrogen halide (HCl, HBr or HI). The hydrogen halide is often dissolved in acetic acid.

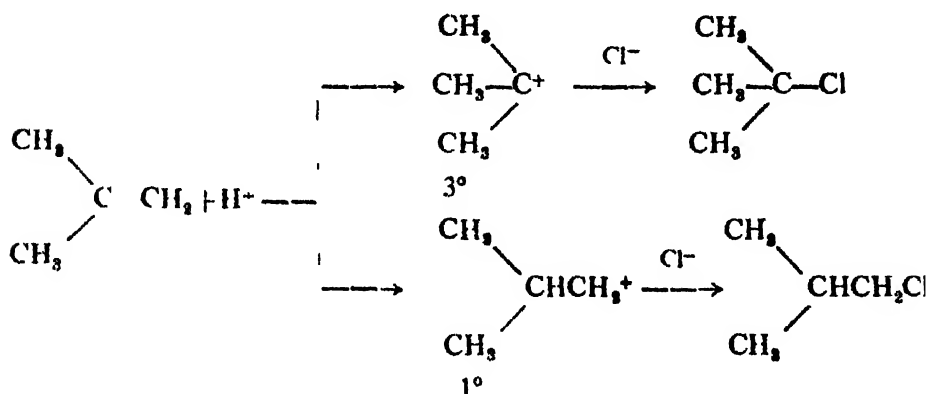


Addition of HX to an alkene is exothermic by -13 to -16 kcal/mole. This addition also takes place in two steps. HCN does not add similar to HBr, because the latter is a stronger acid and a better source of proton.

When a hydrogen halide reacts with a symmetrical alkene, there is only one product possible but in the case of an unsymmetrical alkene there is the possibility of forming two products as shown for *iso*-butylene. Under



these circumstances, the formation of the major product is decided on the basis of a generalization called *Markownikoff's rule*. This rule states that the negative part of the adding species attaches itself to the carbon atom which is more highly substituted (or contains lesser number of hydrogen atoms). This is rationalized in terms of the stability of the intermediate carbonium ion. Consider the addition of HCl to *iso*-butylene. The first step of the reaction is the formation of a carbonium ion. Recall that a tertiary carbonium ion is more stable than a primary carbonium ion, therefore, if



iso-Butylene

the structure, of alkene is such that it can form two different carbocations, it will form the stable one predominantly because the activation required for its formation is low (Fig. 8.3). Thus *t*-butyl chloride is the sole product of the addition.

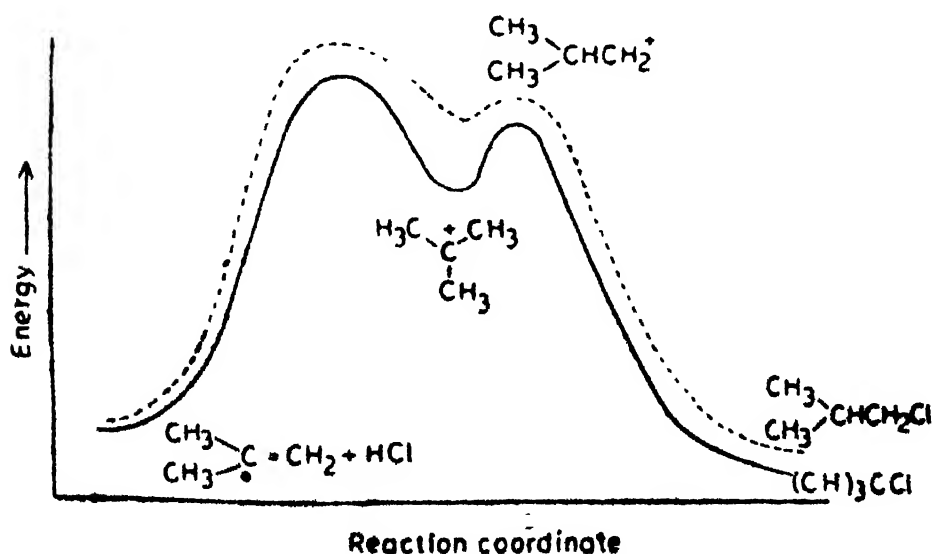
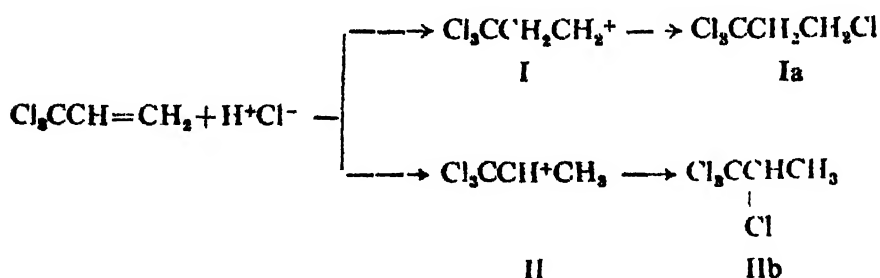


Fig. 8.3 Potential energy diagram for the addition of HCl to *iso*-butylene

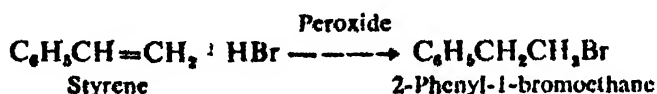
A number of alkenes such as 2-pentene, 1-butene, styrene, etc. obey Markownikoff rule. From the addition of HCl to *iso*-butylene it is noticed that *t*-butyl chloride is formed exclusively, the Markownikoff addition is thus a regioselective reaction. A *regioselective reaction* is one which can potentially yield two or more structural isomers but in practice gives one or predominance of one.

The Markownikoff rule is useful in predicting the products of addition to an alkene. If an electron-pulling group is present at one end of the alkene then the addition is reversed. This is illustrated for this addition of HCl to 3,3,3-trichloropropene.



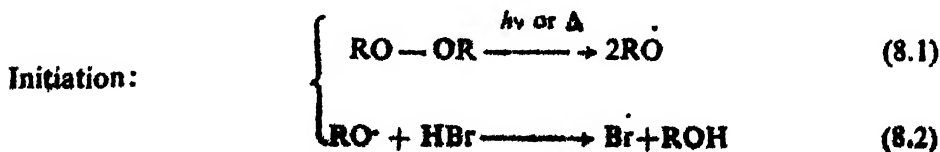
Addition of HCl to 3,3,3-trichloropropene leads to product (Ia) and not (IIb) because the carbocation (I) is more stable than (II) after the addition of a proton to the C=C bond.

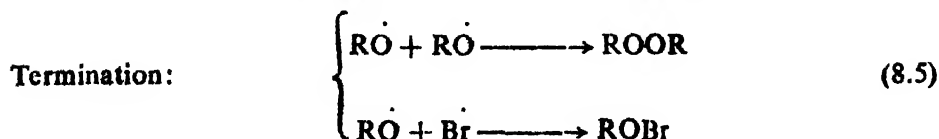
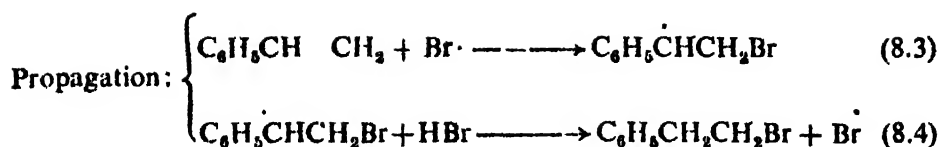
5. *Addition of HBr (Peroxide Effect)*: Addition of HCl and HI takes place according to the Markownikoff's rule but the picture for HBr for long was quite confusing. *Kharasch* discovered that the addition of HBr to an alkene was affected by the presence of peroxides such as benzoyl peroxide or oxygen. Their presence causes the addition of HBr to proceed in an anti-Markownikoff fashion. For instance, addition of HBr to styrene affords 2-phenyl-1-bromoethane and not 1-bromoethylbenzene.



Mechanism

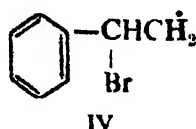
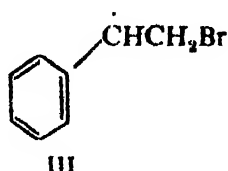
The mechanism of the reaction proceeds *via* a free radical rather than a carbonium ion intermediate. Benzoyl peroxide dissociates into RO^\cdot free radicals which abstracts a hydrogen atom from HBr to generate a free Br radical.





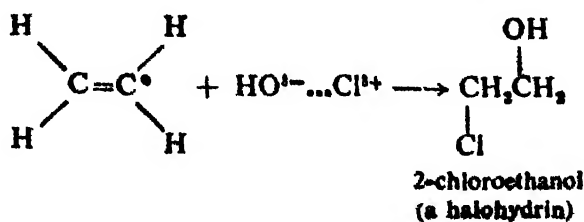
The free radical addition is faster than the heterolytic addition because the chain propagating steps are exothermic.

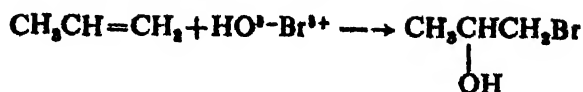
Note that the $\text{Br}\cdot$ radical (rather than H^\cdot in the case of Markownikoff addition) attacks the double bond to produce a free radical as an intermediate. Attack of the $\text{Br}\cdot$ atom can also give rise to two possible free radicals (III) and (IV). The former being secondary is more stable which accounts for the formation of the anti-Markownikoff product.



In this reaction HBr occupies a unique position because HCl and HI do not add similarly to alkenes in the presence of peroxides. The reaction with hydrogen chloride fails because the hydrogen-chlorine bond is too strong to permit an abstraction of the type shown in equation (8.2). Hydrogen iodide has a lower bond energy but the reaction fails here for an entirely different reason. The carbon-iodine bond, in this case is not of sufficient energy to promote a reaction analogous to equation (8.3).

6. *Addition of Hypochlorous Acid:* Halohydrins are produced by the addition of aqueous solutions of halogens such as Cl_2 or Br_2 . In $\text{H}-\text{O}-\text{X}$, the $\text{O}-\text{X}$ rather than the $\text{O}-\text{H}$ bond is broken and the molecule is polarized in the manner $\text{HO}^\delta- \dots \text{X}^{\delta+}$. The halogen thus assumes the role of an electrophile and attacks the double bond. The addition takes place according to the Markownikoff rule and in unsymmetrical alkenes the halogen is attached to the carbon with the greater number of hydrogens.

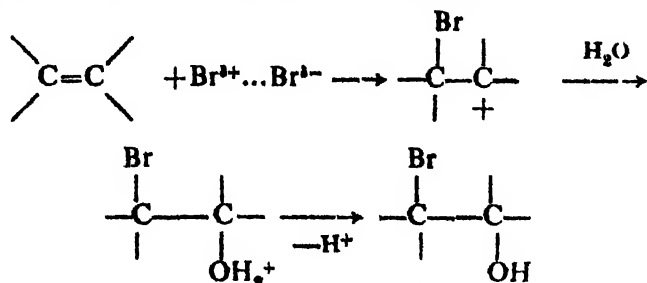




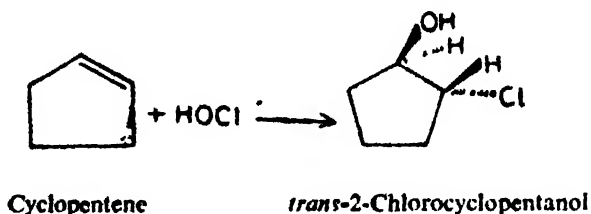
Propylene

1-Bromo-2-propanol
(a bromohydrin)**Mechanism**

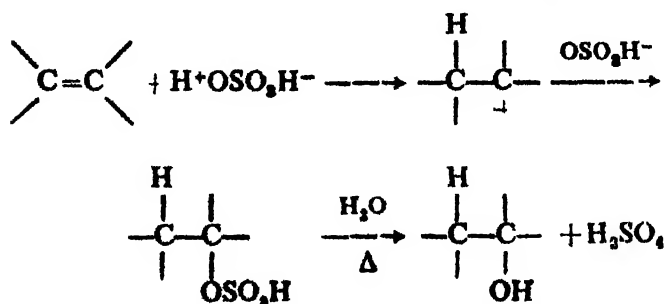
A suitable mechanism for this reaction involves the addition of Br^+ followed by the attack of water and subsequent loss of a proton.



The addition takes place in a *trans* manner analogous to the addition of halogens. Addition of HOCl to cyclopentene thus gives *trans*-2-chlorocyclopentanol.



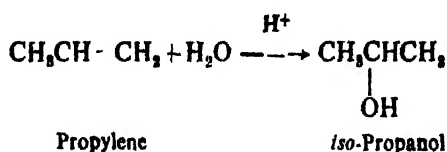
7. Addition of Sulfuric Acid: Cold conc. sulfuric acid adds to olefins to give alkyl hydrogen sulfates in a two step mechanism.



The π -bond being electron rich, accepts a proton from the acid leading to the initial formation of a carbocation. This has only a fleeting existence and in the mixture takes up the negative portion of the acid to form a

stable product. If the alkyl hydrogen sulfate solution is diluted with water and heated an alcohol is produced.

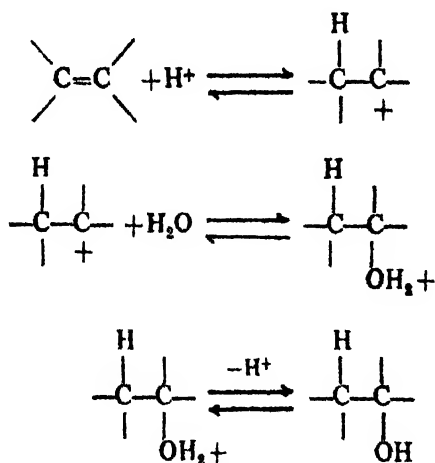
8. *Addition of Water (Hydration)*: Ordinarily, an alkene can be shaken with water indefinitely and nothing will happen. However, if an acid is present in a catalytic amount, a water molecule can be added to the double bond. The resulting product is an alcohol. The process of hydration, i.e., the addition of elements of water is more complicated, than the addition of hydrogen halides, because the reaction is reversible. It is accomplished in the presence of sulfuric acid (60-80%) as a catalyst.



Addition takes place in accordance with the Markownikoff's rule.

Mechanism

The mechanism for the hydration of an alkene in its simplest form can be formulated as follows:

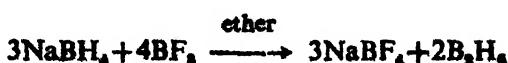


The first step involves the formation of a carbocation by the addition of a proton across the double bond. The subsequent steps involve addition of water and loss of a proton. In hydration, sulfuric acid and not HBr is used as a catalyst because the sulfate ester which is also formed, can easily be hydrolyzed.

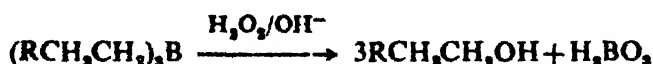
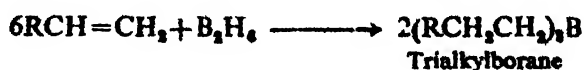
Hydration of alkenes and the dehydration of alcohols are reversible processes and illustrate the principle of *microscopic reversibility*. According to this principle, the forward reaction and its reverse process proceed through the same mechanism, but in opposite directions.

9. Hydroboration: Diborane, B_2H_6 , rapidly adds to a $C=C$ bond to yield a trialkylborane.

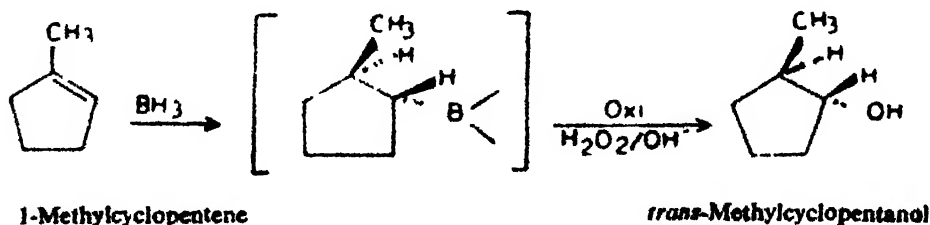
Diborane (a flammable gas) is often prepared *in situ* by the addition of sodium borohydride to boron trifluoride etherate.



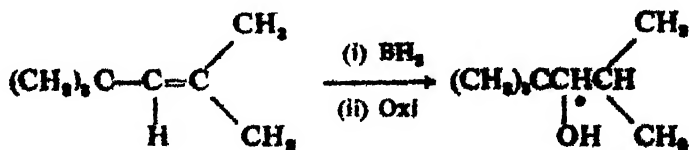
The addition of diborane to an alkene is quantitative and the alkyl boron can be oxidized readily by alkaline hydrogen peroxide to an alcohol. Three molecules of alkene react with one that of BH_3 . This constitutes an important method for the preparation of alcohols and was devised by Prof H.C. Brown of Purdue University, U.S.A., Nobel prize winner (1979).



The addition is controlled by steric factors as the boron atom attacks the less substituted carbon atom, for which reason addition is anti-Markownikoff. Moreover, addition takes place in a *cis* manner. The hydroboration reaction is also highly regioselective because the hydroxyl group always appears at the less substituted carbon atom. This is illustrated by the following example:

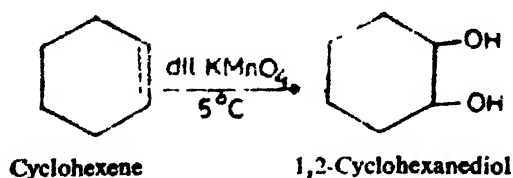


Similarly 2,4,4-trimethyl-2-pentene yields 98% of the alcohol, 2,2,4-trimethyl-3-pentanol.

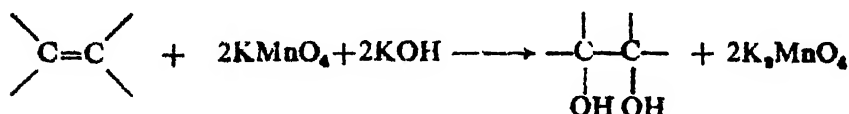


It is especially important to note that a number of other functional groups may be present in an alkene and yet remain unaffected by hydroboration.

10. **Hydroxylation (Glycol Formation):** Cold, dilute and neutral potassium permanganate solution, at low temperature, converts an olefin into a glycol, i.e. a *cis* 1,2-diol. A brown suspension of $\text{Mn}(\text{OH})_2$ appears. A high temperature is avoided since cleavage of the double bond takes place.

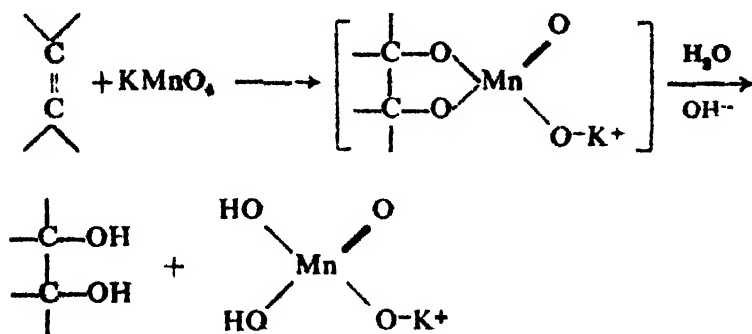


This reaction is frequently employed to detect unsaturation in a molecule as decolorization of the purple color of KMnO_4 occurs on addition of an unsaturated compound and is called the *Baeyer's test*.



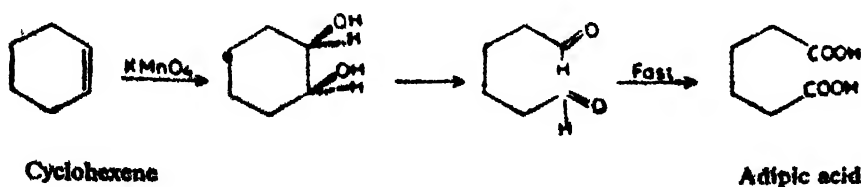
Mechanism

The mechanism involves a cyclic transition state as follows:



The intermediate ester is then cleaved at the dashed lines.

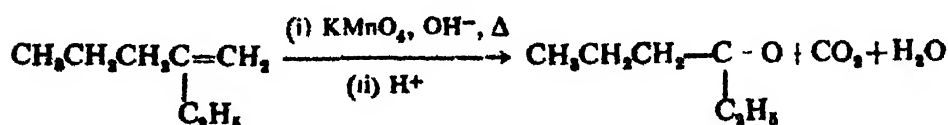
If this reaction is not carried out carefully, further oxidation products are formed, cyclohexene, for instance, forms adipic acid.



The principal use of KMnO_4 oxidation is in the synthesis of acids and in structure elucidation of alkenes. The alkene, for this purpose, is treated with hot potassium permanganate solution and a terminal alkene $\text{H}_2\text{C}=\text{CH}-$, is converted into CO_2 and water, a monosubstituted alkene; $\text{RCH}=\text{CH}_2$, to an acid,

RCOOH ; whereas a disubstituted alkene $\begin{array}{c} \text{R} \\ \diagdown \\ \text{C} = \\ \diagup \\ \text{R} \end{array}$, yields a ketone. For

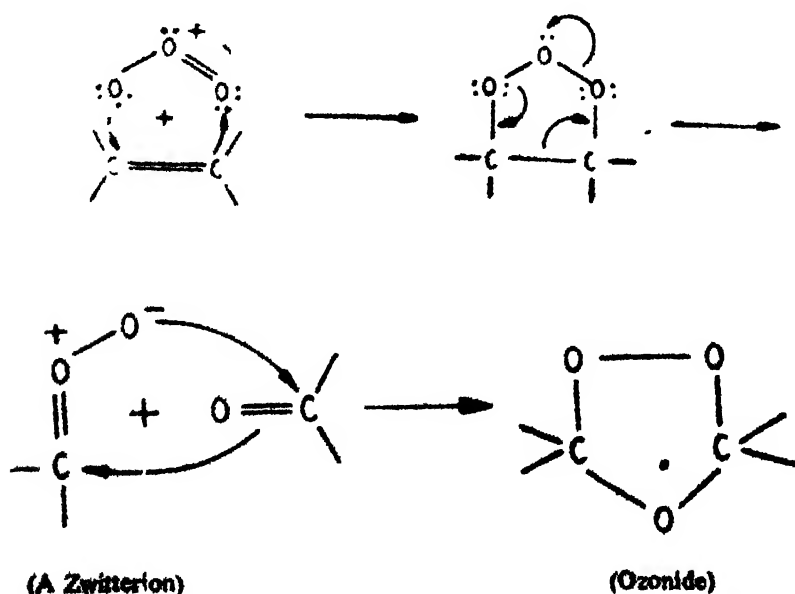
instance, 2-ethylpent-1-ene is converted under these conditions to ethyl propyl ketone.



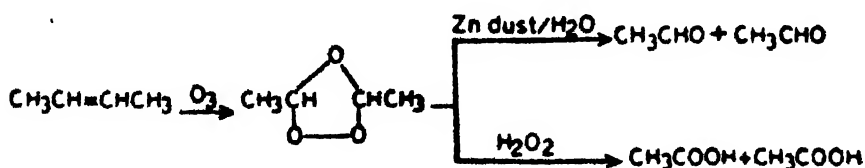
The mechanism of the reaction is believed to involve the formation and cleavage of intermediate glycols.

11. **Ozonolysis:** Alkenes react with ozone in an unusual reaction in which the double bond is completely destroyed to form an ozonide intermediate. This intermediate is highly unstable and is prepared below 20°C in a non-aqueous solvent. Under mild reducing conditions ($\text{Zn}/\text{H}_2\text{O}$) the ozonide gives two new fragments, each of which has a carbonyl group. Under oxidizing conditions (H_2O_2), corresponding carboxylic acids are produced.

This also serves as a method for locating a double bond in a molecule.

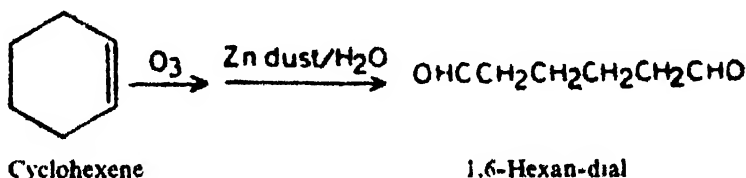


The ozonolysis procedure breaks the C=C bond and attaches an oxygen atom to each of the carbon containing the original double bond. Aldehydes or ketones are formed in the reaction. Ethylene forms only formaldehyde, $\text{H}_2\text{C}=\text{O}$ by ozonolysis; propylene forms both formaldehyde and acetaldehyde, CH_3CHO ; and isobutylene gives acetone $(\text{CH}_3)_2\text{C}=\text{O}$, and formaldehyde. The following products are obtained from 2-butene.

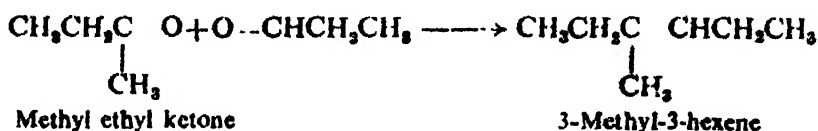


2-Butene

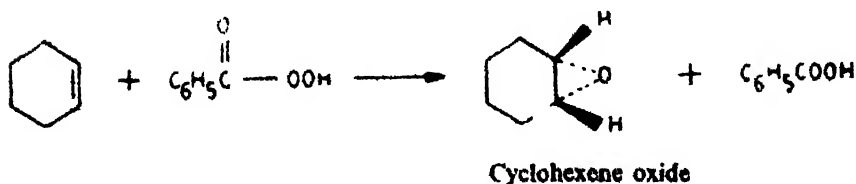
Cyclohexene yields Hexan-1,6-dial on ozonolysis.



Knowing the number and arrangement of carbon atoms in these fragments, one can work back to get the structure of the original alkene. This is demonstrated by the following example:



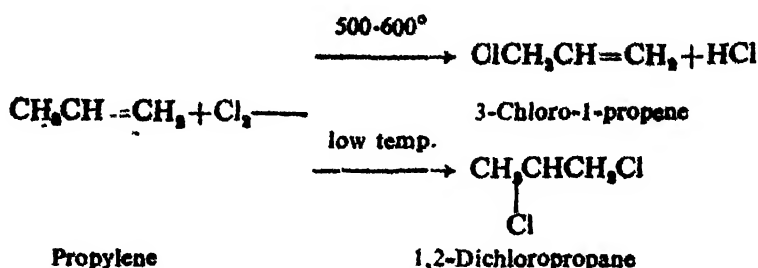
12. **Epoxidation:** Reaction of a peracid with an alkene yields an



oxirane. The reaction is stereospecific *cis*-addition.

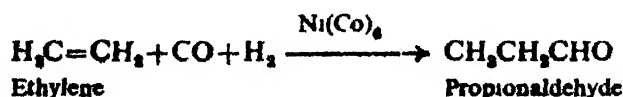
13. **Substitution by Halogens:** An alkene can undergo a substitution rather than addition to the C=C bond by changing the conditions. This is found to be the case when the alkene is heated at 500-600°C in the presence

of halogens. Substitution takes place at the adjacent olefinic carbon atoms.



The substitution reaction probably involves a free radical mechanism.

14. *Oxo Synthesis*: An alkene, on reaction with a mixture of carbon monoxide and hydrogen (water gas), in the presence of nickel carbonyl and under high pressure yields an aldehyde.

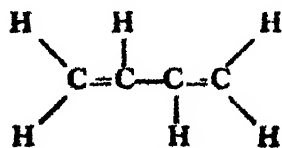


8.5 USES OF ALKENES

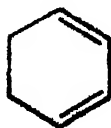
Because of their easy availability and reactivity, ethylenes are used as raw materials in many chemical industries for the preparation of polymers, glycols, aldehydes and other useful products. Isobutylene is used to make *t*-butanol.

8.6 DIENES (DIALKENES)

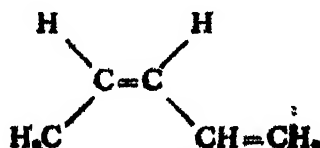
Unsaturated hydrocarbons containing two C – C bonds are called dienes and possess a general molecular formula, $\text{C}_n\text{H}_{2n-2}$. These are isomeric with the alkynes having a corresponding carbon skeleton. Dienes are classified according to the relative positions of the two double bonds. Those dienes which contain an alternate system of single and double bonds are called *conjugated*.



1,3-Butadiene



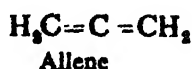
1,3-Cyclohexadiene

*gts*-1,3-Pentadiene

If two or more saturated carbon atoms intervene between the double bonds in a diene then it is termed as an *isolated double bond*.



Hydrocarbons which contain cumulated double bonds are called *annulenes*. Allene is the name given to molecules containing two cumulated double bonds.



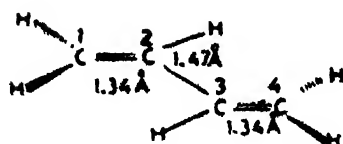
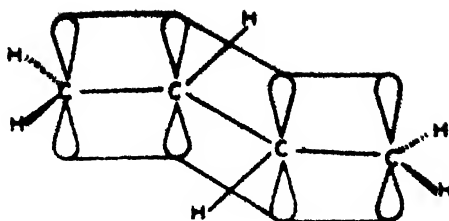
Physical properties of some common dienes are given in Table 8.3.

Table 8.3 Physical Properties of Dienes

Hydrocarbons	Structure	m.p (°C)	b p, (°C)	IUPAC Name
Allene	$\text{H}_2\text{C}=\text{C}=\text{CH}_2$	-146	-32	1,2-Propadiene
Methyl allene	$\text{H}_2\text{C}=\text{CH}=\text{CH}_2$	-136.3	-10.8	1,2-Butadiene
Butadiene	$\text{H}_2\text{C}=\text{CHCH}=\text{CH}_2$	-108.9	-3.0	1,3-Butadiene
iso Prene	$\begin{array}{c} \text{H}_2\text{C}=\text{CCH}=\text{CH}_2 \\ \\ \text{CH}_3 \end{array}$	-145.9	-34.0	1-Methyl-1,3-butadiene
Piperylene	$\begin{array}{c} \text{CH}_3\text{C}=\text{CHCH}=\text{CH}_2 \\ \\ \text{H} \end{array}$	-87.5	-43.0	1,3-Pentadiene
Chloroprene	$\begin{array}{c} \text{H}_2\text{C}=\text{CHCH}=\text{CH}_2 \\ \\ \text{Cl} \end{array}$			2-Chloro-1,3-butadiene

8.6.1 Butadiene

This is also known as 1, 3-butadiene and contains four carbon atoms. The bonding in butadiene seems to be something different than that expected for two isolated $\text{C}=\text{C}$ bonds separated by a single bond. A more plausible representation is one in which the $\text{C}-\text{C}$ bonds have a partially double bond character. In other words, the effect of the π -electrons is spread over the single bonds too. It possesses a resonance energy of the order of 3.5 kcal/mole and is attributed to the extra stability gained due to the C_1-C_3 orbital overlap as shown below.

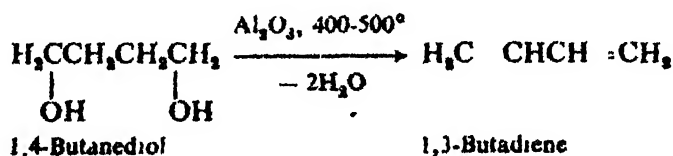
Structural Formula of
1, 3-ButadieneMolecular Orbital Representation of
1,3-Butadiene

Butadiene is a gas at room temperature, b.p. -45° , insoluble in water and possesses no dipole moment. 1, 3-Butadiene is an important monomer.

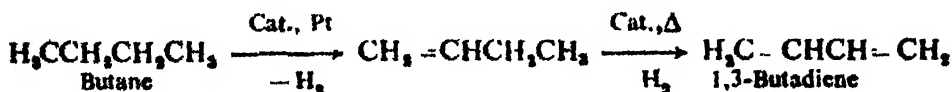
8.6.1a Preparation

1, 3-Butadiene can be prepared by the following methods and generally involves elimination.

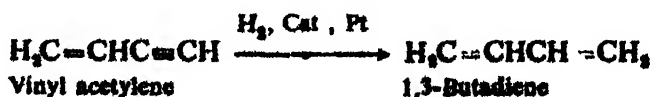
1. *Dehydration of a Diol*: On heating at a high temperature, 1, 4-butanediol in the presence of Al_2O_3 yields 1, 3-butadiene by elimination of two water molecules



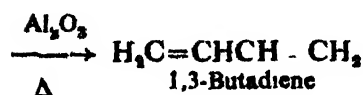
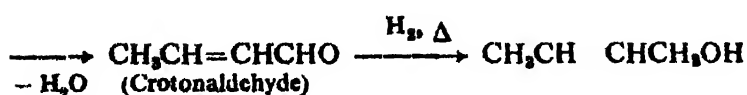
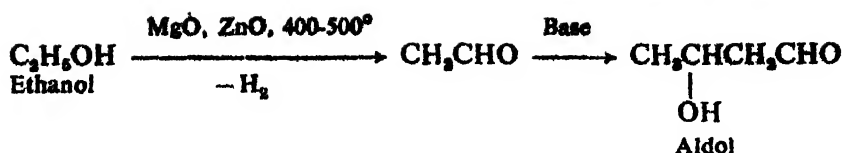
2. *Dehydrogenation*: A two stage dehydrogenation of butane in the presence of chromic oxide catalyst forms 1,3-butadiene.



3. *Hydrogenation*: Partial hydrogenation of vinyl acetylene leads to 1,3-butadiene.



4. *From Ethanol*: 1,3-Butadiene may be prepared from ethanol by the following sequence of steps.

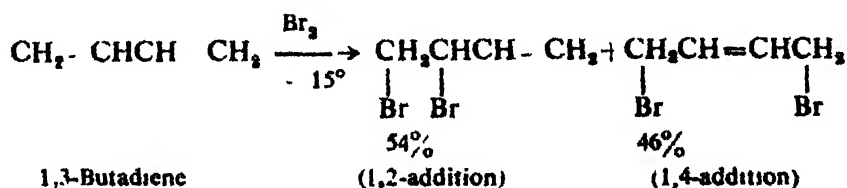


The last step consists of dehydration and isomerization.

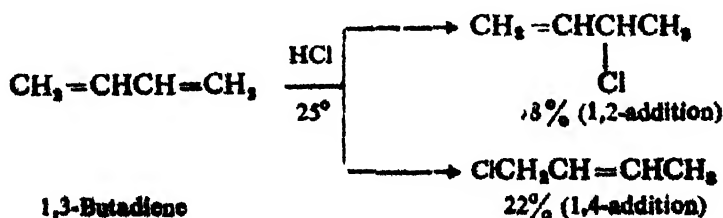
8.6.1b Reactions

The reactions of dienes do not differ in any appreciable manner from those of alkenes.

1. *Addition of Bromine*: Conjugated dialkenes undergo addition in a somewhat unusual fashion, but one that is wholly intelligible in terms of their electronic structure. When 1,3-butadiene is reacted with bromine, there is obtained not only the expected 3,4-dibromo-1-butene but also 1,4-dibromo-2-butene.



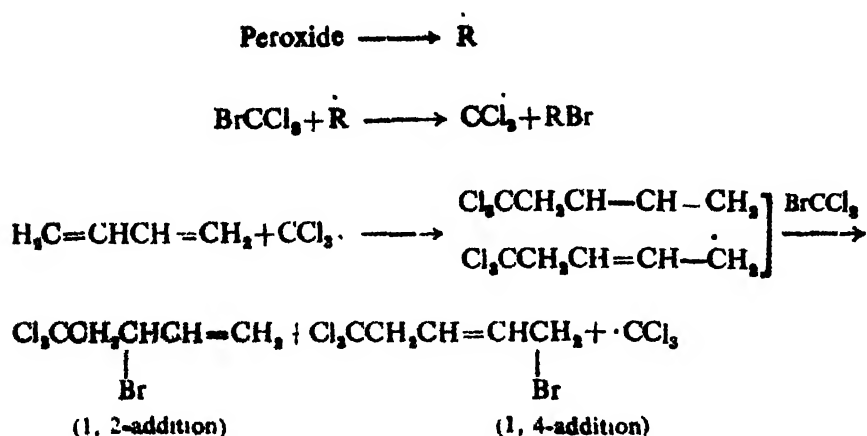
Reactions of this type have been found to be quite general with other conjugated dienes, and 1,4-addition is often the major product of the reaction. Similarly 1,3-butadiene reacts with one mole of HCl or HBr to produce a mixture of two products due to 1,2- and 1,4-addition.



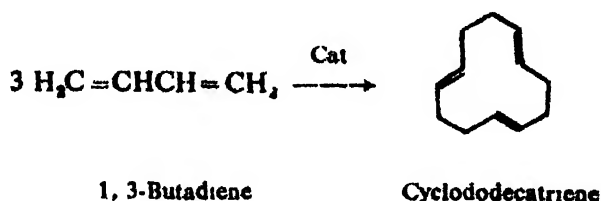
This unusual behavior of 1,3-butadiene is a consequence of the delocalized nature of the intermediate allylic cation. We know that electrophilic addition is a two step process and that the first step takes place in such a way

product. The 1, 4-addition is thus formed in a larger proportion at the expense of the 1, 2-addition product, which is favored energetically. Such a reaction is said to be *thermodynamically* controlled. The formation of the 1, 2-addition product at low temperature is *kinetically* controlled.

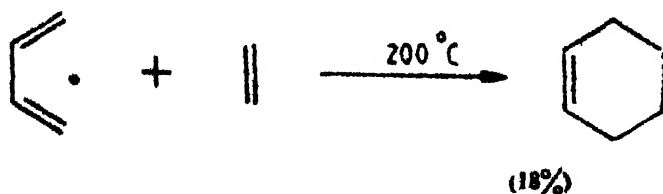
3. *Addition of Free Radicals:* Addition of BrCCl_3 via a free radical process also yields both 1, 2- and 1, 4-addition products.



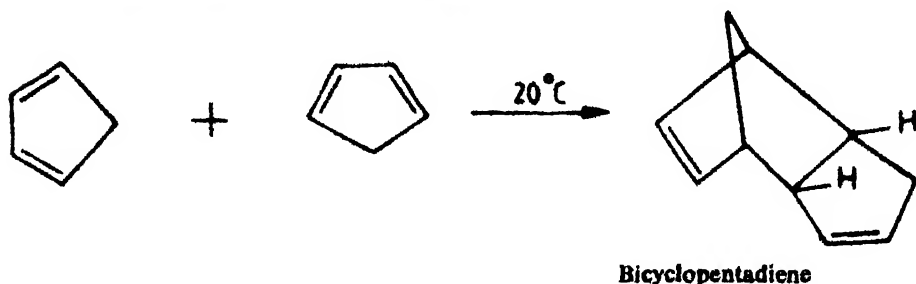
4. *Polymerization:* Butadiene is polymerized in the presence of Ziegler-Natta catalyst [alkyl aluminum and titanium chloride, $\text{Al}(\text{C}_2\text{H}_5)_3 + \text{TiCl}_4$]. Trimerization to a 12-membered ring takes place at the 1, 4-position.



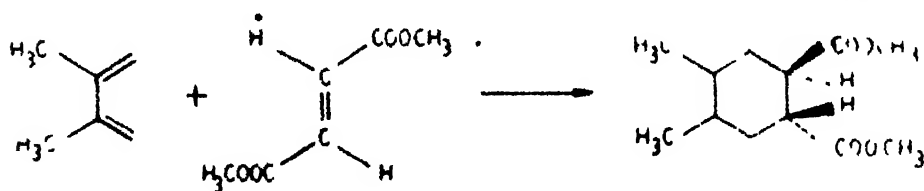
5. *The Diels-Alder Reaction:* An important reaction for the preparation of cyclic compounds in which two unsaturated molecules unite is the *Diels-Alder reaction*. It involves a reaction between a *diene* and an unsaturated compound called a *dienophile*. The simplest reaction of this type is between 1, 3-



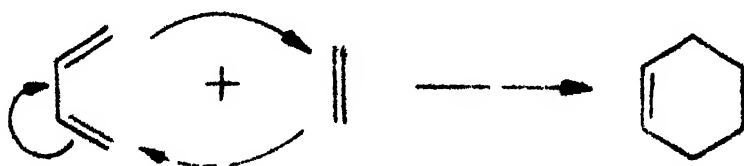
butadiene and ethylene to form cyclohexene. The Diels-Alder reaction is a (4+2) cycloaddition reaction. It can be carried out with or without a solvent and may be initiated by heat, light or AlCl_3 catalyst. Presence of electron-withdrawing groups such as $-\text{COOH}$, $-\text{COOR}$, $-\text{NO}_2$, $-\text{CN}$ activates the dienophile and accelerates the rate of the reaction. Dienes are activated by electron-donating groups such as $-\text{OCH}_3$, $-\text{CH}_3$, $-\text{N}(\text{CH}_3)_2$. Some reactive dienes, however, do not require the presence of activated dienophiles. One such example is cyclopentadiene.



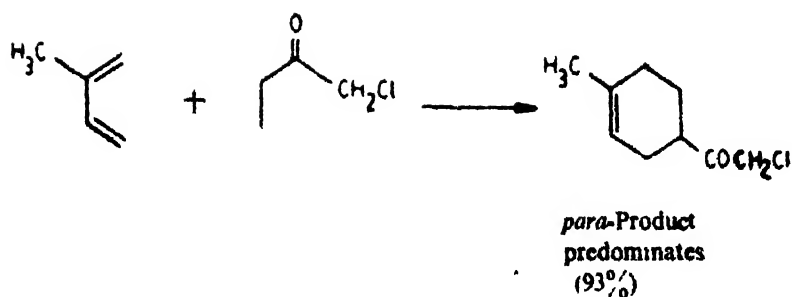
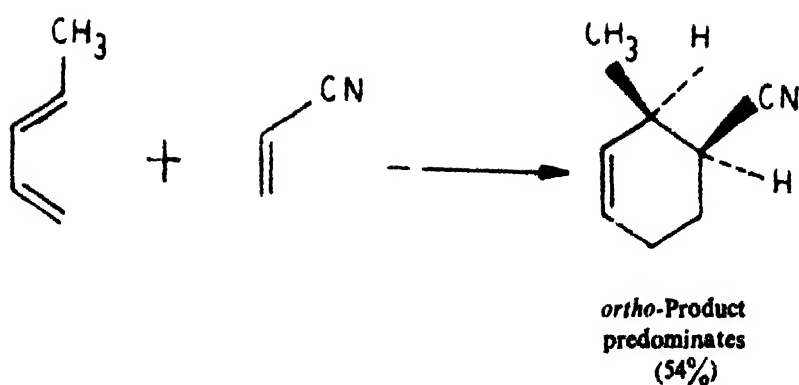
The Diels-Alder reaction displays a stereospecific pathway, i.e., the stereochemistry of the dienophile is preserved in the product. In other words, the addition takes place in a *cis*-manner. The reaction, for example, between 2,3-dimethyl-1,3-butadiene and dimethyl fumarate yields the *trans*-adduct in which the ester functions are still *trans* to each other.



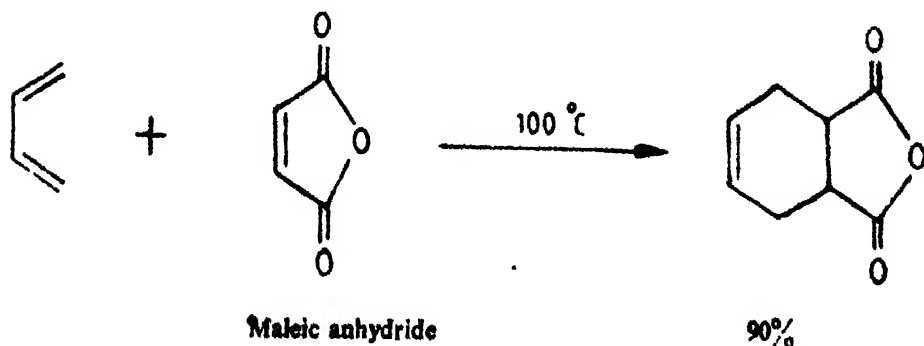
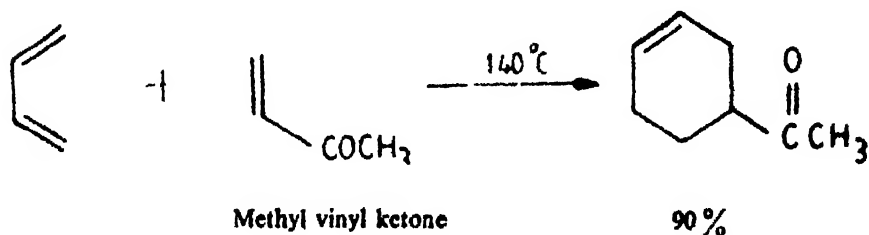
The reaction is second order and is not affected by the presence of polar solvents. Therefore, a concerted cyclic mechanism has often been preferred

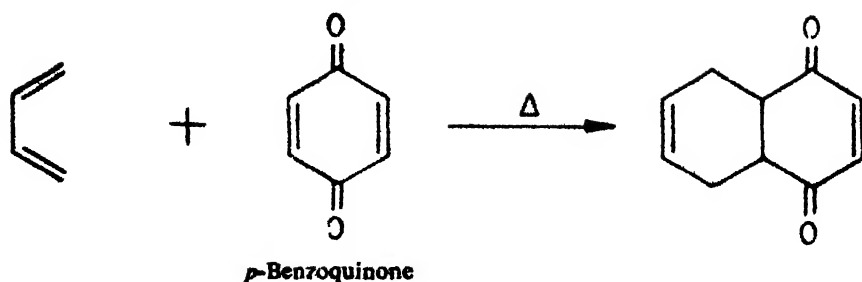


for this reaction. The Diels-Alder reaction is also considered to be regio-selective when both the dienes and the dienophiles are unsymmetrically substituted. It has been observed that there is a preference for *ortho*- and *para*-products as shown below:

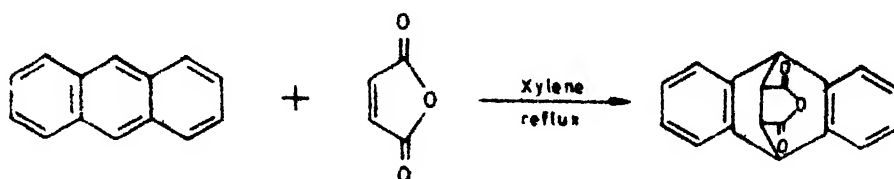


A wide variety of dienophiles can participate in the Diels-Alder reaction. These are generally derivatives of ethylene and acetylene.

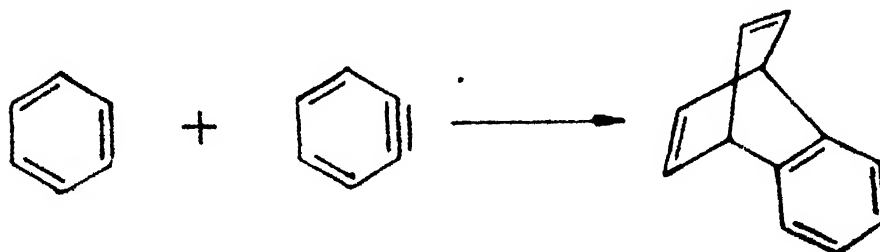




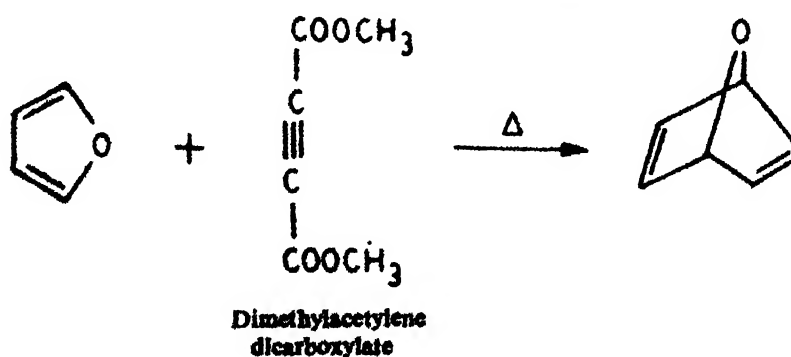
Many polycyclic hydrocarbons react with dienophiles by 1,4-cyclo addition. This reaction is particularly of interest with anthracene and maleic



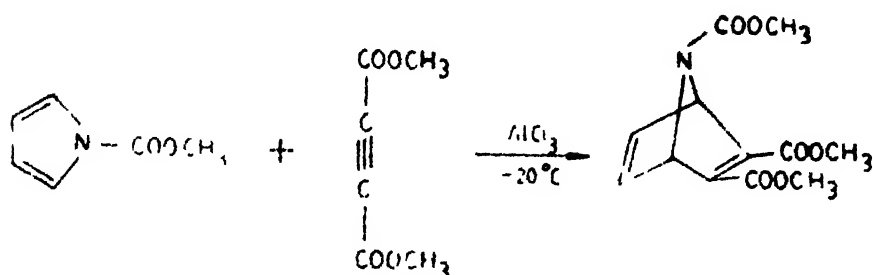
anhydride. Even aromatic compounds such as benzene which are generally inert, undergo Diels-Alder reaction with reactive dienophiles such as



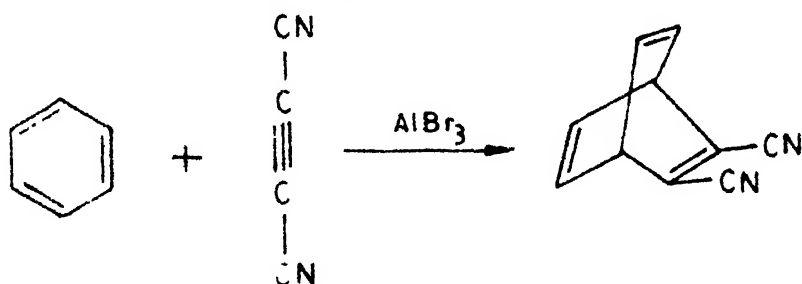
benzene. Among the five-membered heterocyclic rings, only furan has diene-like character and participates in the Diels-Alder reaction. Pyrrole containing



electron-withdrawing groups at 1-position undergoes Diels-Alder reaction particularly in the presence of Lewis acid catalysts. Many of these adducts are valuable synthetic intermediates.

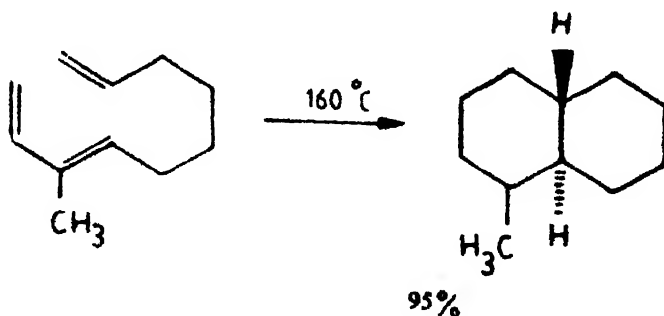


Lewis acids enormously accelerate the Diels-Alder reaction. Even benzene reacts with dicyanoacetylene in the presence of AlBr₃. In the



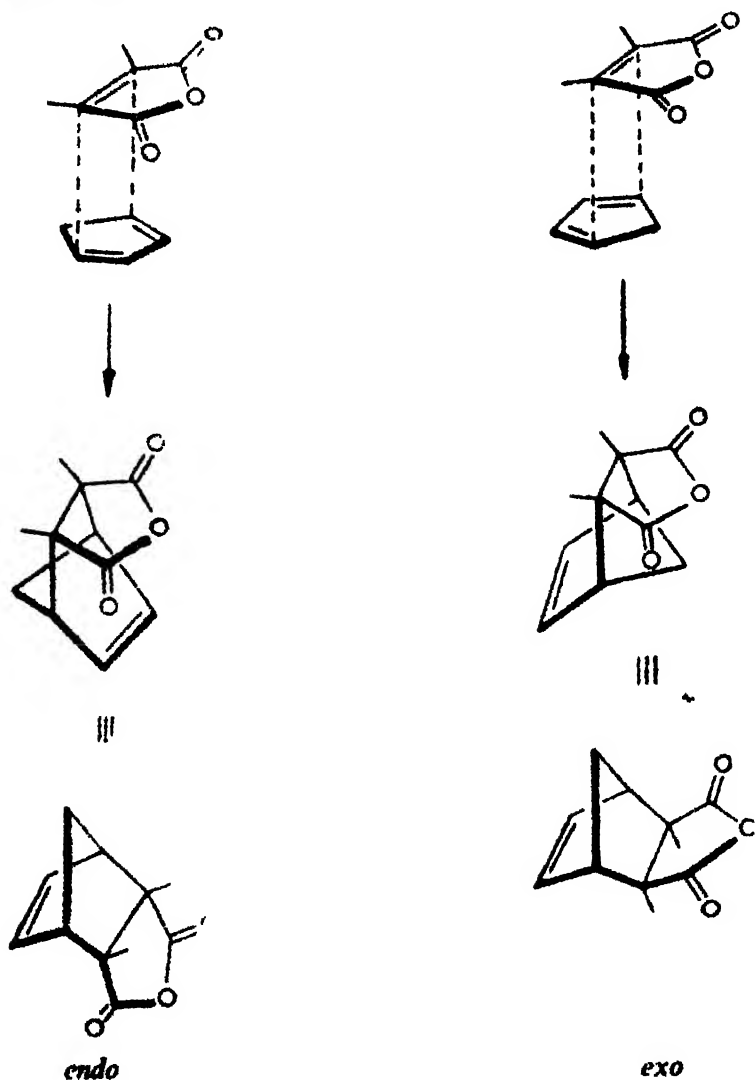
absence of AlBr₃, severe heating is necessary for the reaction and the yields are low.

The intramolecular variant of the Diels-Alder reaction has been known for a long time and has found applications in the synthesis of natural products. It is exemplified by the accompanying reaction. An interesting feature



of the Diels-Alder reaction is that a mixture of two products namely *endo* and *exo* is obtained. This has been explained on the basis of *Alder's rule of endo addition*. This rule states that the two components arrange themselves in parallel planes and addition takes place from that orientation which has the maximum accumulation of double bonds. Thus the structure of the product can nearly be predicted by placing the reactants in two parallel planes in such a way as to obtain maximum overlapping of double

bonds. This is demonstrated for the reaction between cyclopentadiene and maleic anhydride.



Most dienes and dienophiles give a mixture of both *endo*- and *exo*-isomers under ordinary experimental conditions in the Diels-Alder reaction.

QUESTIONS

8.1 Give formulas corresponding to the following names:

- 3-Chloro-3-phenyl-1-butene
- 4-Nonene
- 2,3-Dimethyl-2-pentene
- 2,3-Dimethyl-1,3-butadiene
- 1,4-Dibromobut-2-ene

f. *cis*-2-Pentene

g. 1,3-Dimethylcyclopentene

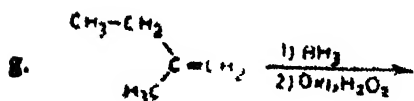
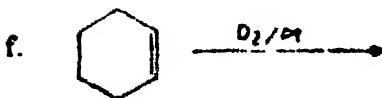
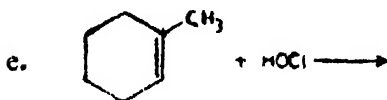
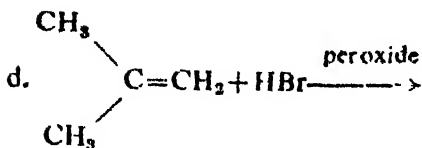
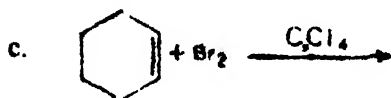
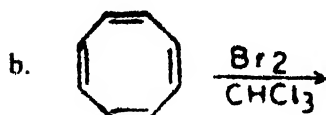
h. (z)-1,3-Pentadiene

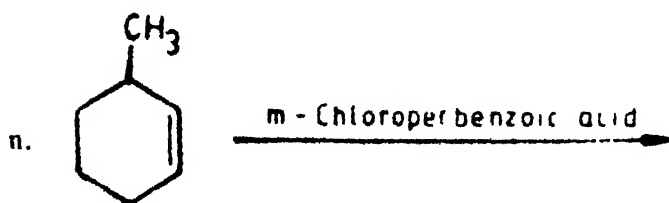
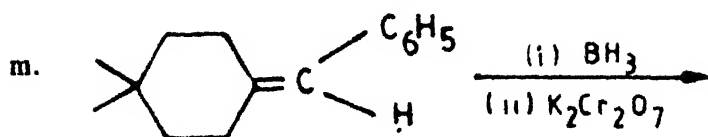
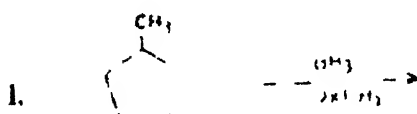
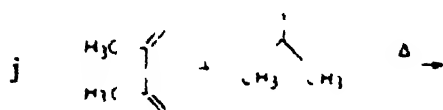
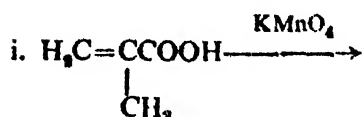
i. z-and-E-2-phenyl-2-butene

- 8.2 Illustrate by means of structural formula or an equation the meaning of the following:

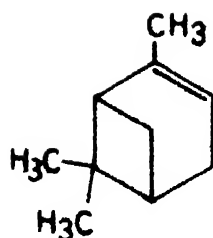
Markownikoff's rule, a conjugated diene, hydroboration, hydration, *cis*-addition process.

- 8.3 When maleic acid is treated with bromine, the 2,3-dibromosuccinic acid can be resolved into its enantiomers. But the addition of bromine to fumaric acid yields 2,3-dibromosuccinic acid which is non-resolvable. What do these observations indicate regarding the mechanism of bromine addition?
- 8.4 Write the product of the following reactions and justify your answer:

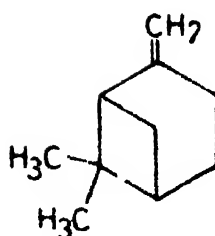




- 8.5 A 10 g mixture containing butane and 2-butene reacts with 8.0 g of bromine dissolved in carbon tetrachloride. Calculate the percentage of butane in the mixture.
- 8.6 Compound A, $\text{C}_6\text{H}_{14}\text{O}$, on treatment with hot sulfuric acid yields an unsaturated compound B, C_6H_{12} , which on ozonization gives a mixture of carbonyl compounds C, $\text{C}_2\text{H}_4\text{O}$ and D, $\text{C}_3\text{H}_6\text{O}$. Deduce the structures of A, B, C and D.
- 8.7 Write a short note on the utility and mechanism of the Diels-Alder reaction.
- 8.8 How will you distinguish between (A), and (B) using ozonolysis.



A

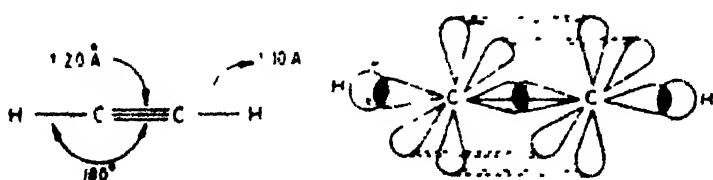


B

- 8.9 Which of the hybridized carbon atoms are present in 1,2-butadiene:
- Only sp hybridized carbon atoms
 - sp , sp^2 and sp^3 hybridized carbon atoms
 - Only sp^2 hybridized carbon atoms
 - Both sp and sp^3 hybridized carbon atoms.
- 8.10 Give the preparation and properties of 1, 3-butadiene.
- 8.11 a. Describe the mechanism of the addition of a halogen acid to an alkene.
b. Discuss the mechanism of the addition of HBr to propene.
- 8.12 Explain with a suitable example the 1,4 addition to 1, 3-butadiene.
- 8.13 What evidence is there to show that the addition of halogens to a double bond is a two step mechanism ?
- 8.14 Describe the Diels-Alder reaction.
- 8.15 Explain the following:
- anti*-Markownikoff addition to alkene is possible in case of HBr only.
 - Addition of bromine to alkenes is a two step process.
- 8.16 Explain why HCN does not add to an alkene as does HBr
- 8.17 Why does HBr add to 1,3-butadiene to give both 1,2- and 1,4-addition products.

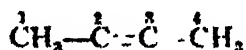
Alkynes or Acetylenes

The alkynes are also unsaturated hydrocarbons that contain a carbon-carbon triple bond and possess the general formula C_nH_{2n-2} . The first member of the series is acetylene, $HC\equiv CH$, and the class as a whole is also referred to *acetylenes*. The carbon atoms in acetylene are in an sp hybridized state. The σ -bond is formed by the end-on overlap of the sp hybrid carbon orbitals. The remaining $2p_x$ and $2p_y$ orbitals on each carbon atom which are mutually perpendicular to the carbon-carbon bond overlap to form π -bonds. The C—C bond distance is still shorter compared to ethylene or ethane and is 1.20 \AA . It is a linear molecule, the bond angle being 180° , and there is no geometric isomerism possible about this functional group. Acetylenes contain a triple bond which is made of one σ - and two π -bonds.

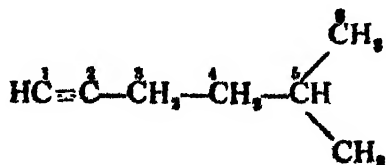


9.1 NOMENCLATURE OF ACETYLENES

Acetylene, the common name for ethyne is unfortunate since the ending *-ene* suggests a double bond. The general rules stated in Sec. 2.3, also apply in naming alkynes. The suffix *-ane* is changed to *-yne* and the position of the triple bond is specified by a number. This is illustrated by the following examples:

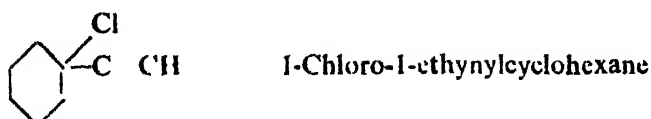


2-Butyne (But-2-yne)



5-Methyl-1-hexyne
(5-Methylhex-1-yne)

In complex structures the alkynyl group is used as a modifying prefix.



9.2 PHYSICAL PROPERTIES OF ALKYNES

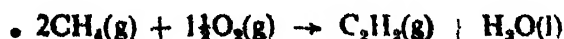
The boiling points normally increase with the increase in the carbon content (Table 9.1); the branched acetylenes have a low boiling point. Alkynes, like alkanes and alkenes are non-polar and are insoluble in water or ethanol but soluble in ether, benzene and carbon tetrachloride

Table 9.1. Physical Properties of Alkynes

Hydrocarbon	Structure	m p (°C)	b p (°C)	Density
Acetylene (Ethyne)	HC ≡ CH	82	-75	
Methylacetylene (Propyne)	HC ≡ CCH ₃	-101.5	-23	
Ethylacetylene (1-Butyne)	HC ≡ CCH ₂ CH ₃	-122	9	
Dimethylacetylene (2-Butyne)	H ₃ C ≡ CCH ₃	-24	27	
<i>iso</i> -Propylacetylene (3-Methyl-1-butyne)	$\begin{array}{c} \text{CH}_3 \\ \\ \text{HC} \equiv \text{CCHCH}_3 \end{array}$		29	
Propylacetylene (1-Pentyne)	HC ≡ CCH ₂ CH ₂ CH ₃	-98	40	
Butylacetylene (1-Hexyne)	HC ≡ CCH ₂ CH ₂ CH ₂ CH ₃	-124	72	0.7152

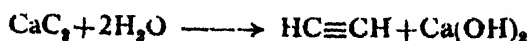
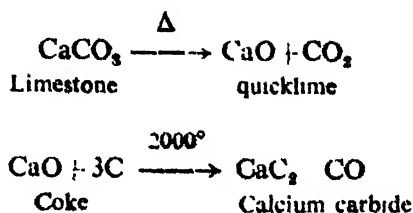
9.3 PREPARATION OF ALKYNES

Acetylene is manufactured industrially from natural gas. The partial combustion of methane, the principal component of natural gas, yields acetylene.



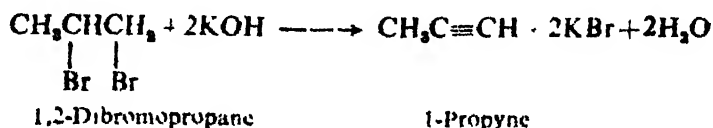
1. *From CaC₂*: In the laboratory, acetylene can be prepared from calcium carbide which is obtained readily by heating a mixture of quicklime (CaO) and coke (carbon) in an electric furnace. Calcium carbide is

decomposed to acetylene with water. This method is used industrially. Acetylene so prepared is not pure.

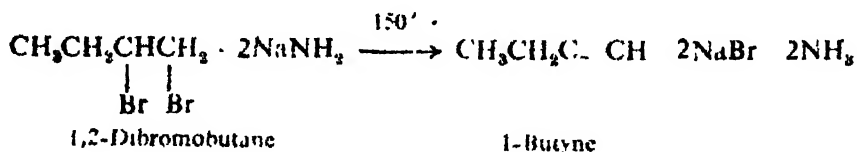


The main disadvantage of this method is its high energy consumption.

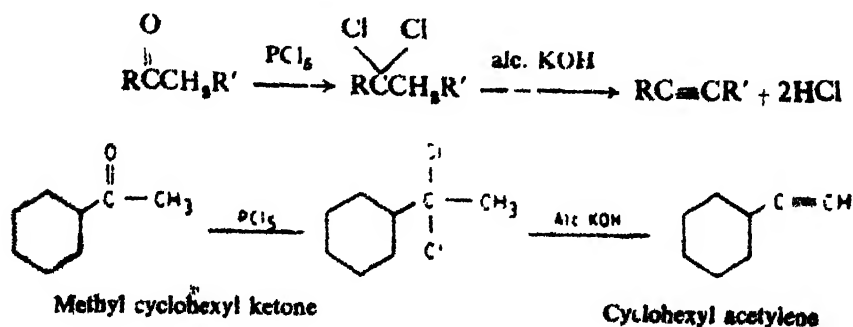
2. *Dehydrohalogenation of Vicinal Dihalides*: The vicinal dihalides on reaction with alc. potassium hydroxide solution or sodamide yield acetylene:



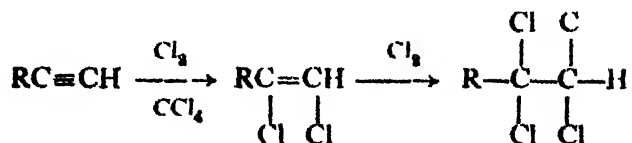
If 1-alkynes, other than propyne, are needed then the procedure is modified by substituting NaNH_2 or KNH_2 for alc. KOH because this latter reagent isomerizes 1-alkynes to 2-alkynes



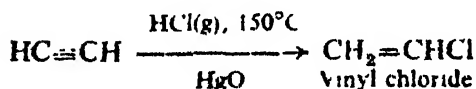
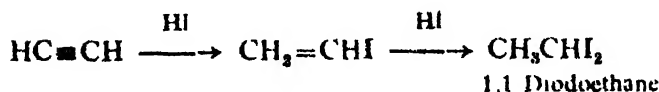
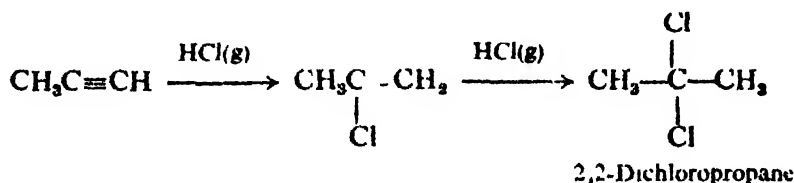
3. *From Ketones*: Phosphorus pentachloride reacts with a ketone and replaces the oxygen atom by two chlorine atoms to yield a geminal (i.e., in which the chlorine atoms are present on the same carbon atom) dichloride. This on treatment with alc. potassium hydroxide forms acetylene by elimination of two HCl molecules.



2. *Addition of Halogens:* Alkynes react with two moles of halogens to form tetrahalo derivatives, as the final product.

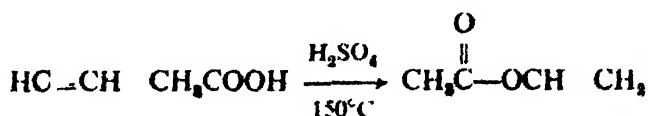


3. *Addition of Hydrogen Halides:* Hydrogen chloride, hydrogen iodide and hydrogen fluoride add to alkynes. A *gem*-dihalide product is formed.

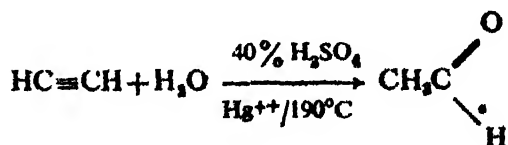


The addition takes place by the initial formation of a vinyl cation. A second mole of the acid adds and addition follows Markownikoff rule.

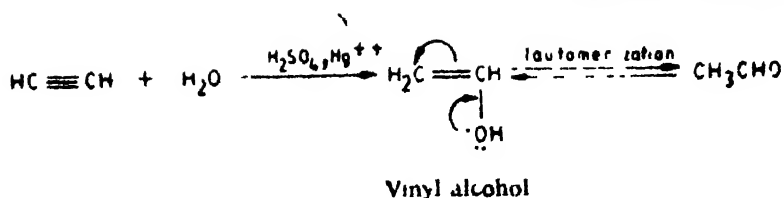
4. *Addition of Acetic Acid:* Acetic acid adds to acetylene to form ethenylethanoate which can be polymerized to polyvinyl acetate (PVA).



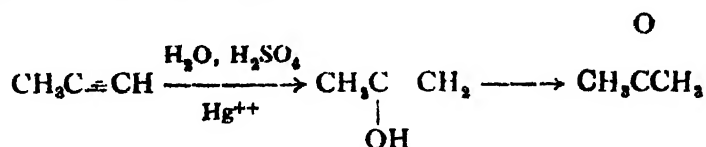
5. *Addition of Water:* Because acetylene is available in large quantities, it is used as a cheap raw material for the manufacture of chemicals, particularly acetaldehyde. This is done by the addition of water to a triple bond in the presence of sulfuric acid and mercuric sulfate as catalyst. The mercuric ion, Hg^{++} , coordinates with the triple bond and thus facilitates the



addition of water. This results in the formation of an enol (one + ol). A water molecule adds in accordance to Markownikoff's rule. Vinyl alcohol and



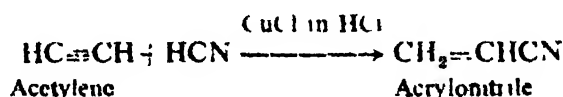
acetaldehyde are in tautomeric equilibrium; but the keto form predominates as the >C=O isomer is lower in energy by 15 kcal/mole. Ketones can similarly be obtained from acetylene homologues, for instance, acetone is obtained from methylacetylene.



Ethanol adds to acetylene to give ethoxyethene.

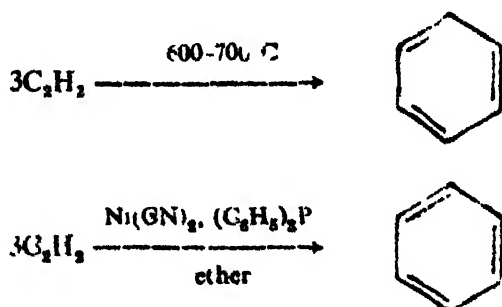


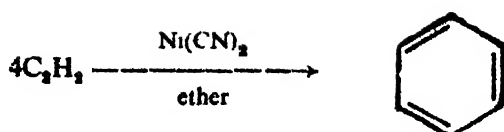
6. *Addition of HCN:* Several simple molecules like HCN do not add rapidly to alkenes but can be added to acetylenic triple bond in the presence of a catalyst ($\text{CuCl} + \text{HCl}$). From acetylene and HCN an important monomer, acrylonitrile is obtained.



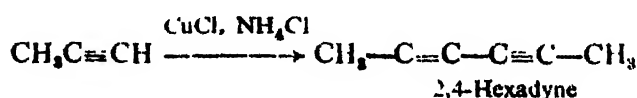
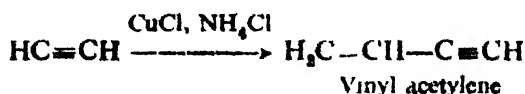
Acrylonitrile copolymerizes with 1,3-butadiene to form synthetic rubber Buna N

7. *Cyclization of Acetylene* Acetylene on prolonged heating at 600–700°C yields benzene and related compounds in low yields. Using transition metal catalysts cyclization can be carried out under milder conditions and in higher yields.



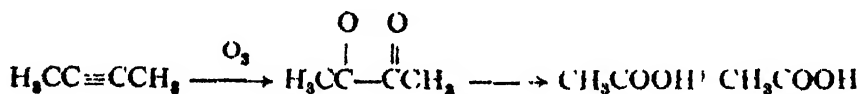


Acetylene and homologs dimerize in the presence of copper salt and ammonia (or ammonium chloride).

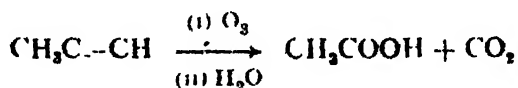


Polymerization of acetylene to linear polyolefin has not been successful.

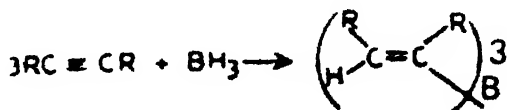
8. *Reaction with Ozone:* Ozonolysis of alkynes produces two molecules of carboxylic acids with the cleavage of the carbon-carbon triple bond.



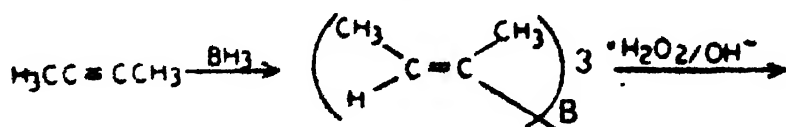
A terminal carbon, on the other hand, is oxidized to carbon dioxide and an acid.



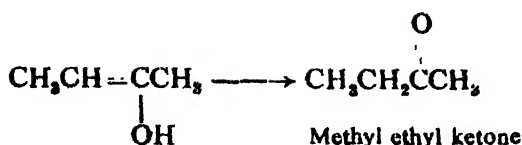
9. *Hydroboration:* Diborane adds only once to alkynes that have an internal triple bond



The resultant trivinylboranes react with a number of reagents to give useful products. The C—B bond of the vinylborane can be broken oxidatively (alkaline H_2O_2); the initial product is a vinyl alcohol that rearranges rapidly to the corresponding aldehyde or ketone.

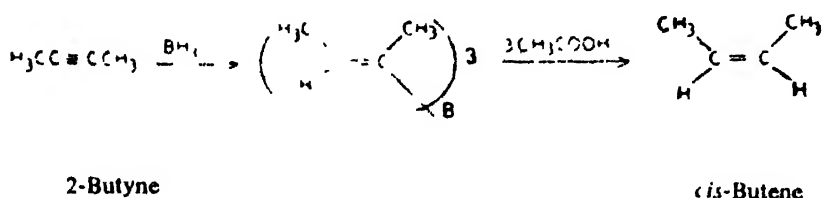


2-Butyne

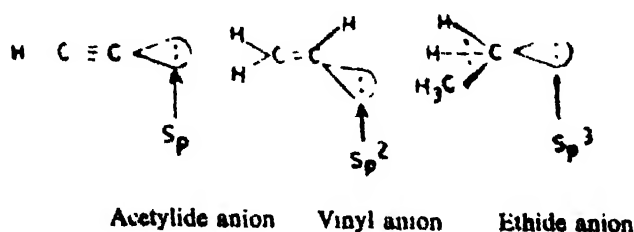


With terminal alkynes, aldehydes are formed. As seen earlier, alkenes yield only alcohols.

The trivinylboranes also undergo protonolysis to give *cis*-alkenes.



10. *Formation of Acetylides:* Acetylide formation is characteristic of alkynes bearing a terminal hydrogen atom, i.e. $\text{RC}\equiv\text{CH}$. The hydrogen can be removed as a proton by a strong base leading to a relatively stable anion $\text{RC}\equiv\text{C}^-$. The anion formation does not take place in the case of ethylene or ethene. This difference may be explained in terms of the character of the orbital occupied by the lone pair electrons in the three anions. In $\text{RC}\equiv\text{C}^-$ anion the electron pair is contained in an sp orbital, in vinyl anion the lone pair is in an sp^2 orbital while in ethide anion (C_2H_5^-), they occupy sp^3 orbital. An electron in the s orbital is more tightly held than in a p orbital because the s -electrons are closer to the nucleus. Since there is more s -character in an sp orbital the acetylene sp orbitals are more electronegative. The acetylide anion is thus more stable because sp carbon is most electronegative. In other words, the carbon is best able to accommodate an electron pair in the anion and as a result acetylene is acidic. The acidity of an

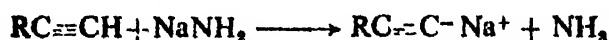


alkyne, however, is slight as it does not turn blue litmus red. The greater the s -character of hybridized orbital, the more acidic is the proton or less

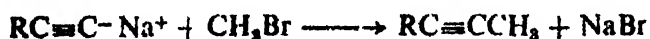
basic is that pair of electrons. The acidity decreases in the following order:



Acetylides formation with alkali metals: Sodium acetylide and other sodium alkynides can be prepared by treating terminal alkynes with a base such as sodium amide in liquid ammonia. These are acid-base reactions. Sodium alkynides are useful intermediates in the synthesis of acetylene

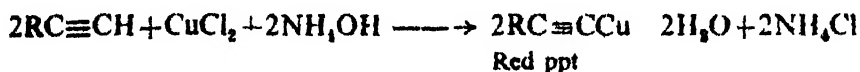


homologues. This is done by treating the sodium alkynide with a primary alkyl halide.

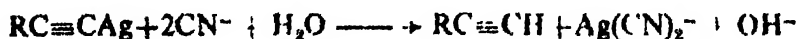


In such reactions the alkynide anion acts as a nucleophile and displaces the halide ion from primary alkyl halide.

Acetylide formation with heavy metals: Acetylene and other alkynes containing a terminal hydrogen atom also form acetylides or alkynides with silver and copper ions.



These alkynides are insoluble in water and have characteristic colors. Their formation is used as a qualitative test to demonstrate the presence of acetylenic hydrocarbons with a terminal hydrogen and to distinguish them from alkenes. An internal alkyne such as $\text{RC}\equiv\text{CR}$ will not react. Acetylene reacts with NaNH_2 to form sodium ethynide ($\text{NaC}\equiv\text{CNa}$), with Copper (I) salt, Copper ethynide ($\text{CuC}\equiv\text{CCu}$) and silver ethynide ($\text{AgC}\equiv\text{CAg}$) with silver nitrate. These acetylides are potential explosives in the dry state and must be handled with care. The terminal alkyne can be regenerated by treating the acetylide with NaCN or with a strong acid.



9.5 USES OF ALKYNES

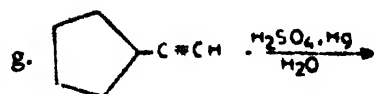
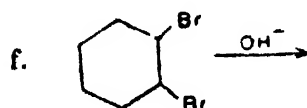
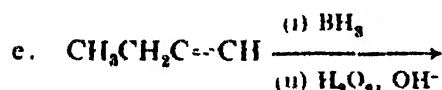
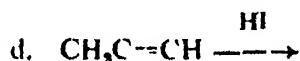
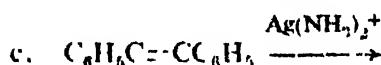
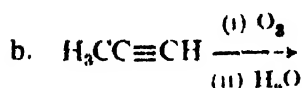
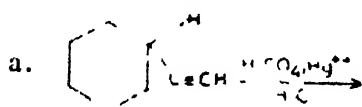
Combustion of acetylene with oxygen produces an intensely hot flame and thus large quantities of acetylene are used for cutting and welding of metals. Acrylonitrile once prepared by the addition of HCN to acetylene [$\text{CuCl}/\text{NH}_4\text{Cl}$, catalyst] is an important raw material for textile fibres such as Orlon and Acrilon. Acetylene is also used as an illuminant and is a source of many basic chemicals like acrylic acid, ketones, etc.

QUESTIONS

9.1 Write structures for the following compounds:

- But-2-yn-1,4-diol
- Vinylacetylene
- 1,4-Dichlorobut-2-yne
- 3-Benzyl-1-bromo-1-pentyne
- 1-Sodiopropyne
- 6-Dodecyne
- trans*-2-Hexen-4-yne
- 3,3-Dimethyl-1-butyne

9.2 Write the products and justify your answer:



- 9.3 A hydrocarbon has the formula corresponding to that of an alkyne, $\text{C}_n\text{H}_{2n-2}$, but it adds only one molecule of bromine per mole of the hydrocarbon. What type of structure does the hydrocarbon have?
- 9.4 In what ways do alkynes differ from alkenes? What similarities are recognized in the two classes of hydrocarbons?
- 9.5 A compound contains C = 88%, H = 12% and its molecular weight is 82. One mole of the compound absorbs two moles of bromine and when it is shaken with CuCl in ammonia, the compound produces a precipitate containing copper. Draw the structure of the compound.

- 9.6 A cylinder contains one of the following gases: propane, propene or propyne. What chemical tests would you apply to identify the gases?
- 9.7 Hydration of an alkyne gave methyl propyl ketone. What formula would you assign to the alkyne?
- 9.8 Write the formula for each of the isomeric hydrocarbons, C_4H_6 , which contain a triple bond. Suggest names according to IUPAC system of nomenclature.
- 9.9 Starting with acetylene and any other reagent show how would you obtain the following:
- $CH_3CH_2C\equiv CH$
 - CH_3CH_2COOH
 - $CH_3CH_2CH_2CH_3$
 - $CH_3C(CH_3)_2CH_2CH_3$
 - $CH_3CH(Br)CH_3$
 - $CH_3=CHCH_3$
- 9.10 Write a short note on the orbital picture of acetylene.
- 9.11 Write the products when propyne is treated with; acetic acid, H_2O/H^+ , BH_3 , C_2H_5OH , HCl and O_3 .
- 9.12 With pertinent chemical equations show the product of hydroboration and subsequent oxidation (H_2O_2) of propene and propyne.

Polymers

Organic chemistry has made valuable contributions in the field of polymers, dyes, drugs, detergents, agricultural chemicals and cosmetics. This chapter would be concerned with the synthesis and applications of polymers. A *polymer* (from the Greek, *poly* meaning many) may be described as a long molecule formed by linking together a number of smaller molecules. The smaller molecule is called a *monomer*. The bonding in each polymer molecule is covalent. The polymers possess a high molecular weight of several thousand. Polymers nowadays are not difficult to prepare because of the easy availability of the raw materials. Most of the synthetic polymers are of recent origin but they have made an impact on our daily life. They have found extensive applications in textile fibres, rubber and rubber goods, building materials, packaging, fancy decorating articles and ion-exchange resins.

10.1 NATURAL AND SYNTHETIC POLYMERS

Polymers are classified according to their origin or source. Those obtained from natural sources such as animal or plant are *natural polymers*. These are also made by linking together smaller units. Carbohydrates, for instance, are made by linking glucose molecule, proteins (wool, silk and hair) are made by linking α -amino acids and natural rubber contains isoprene units. Many of the natural polymers occur in the biological system and are termed as *biopolymers*. Nucleic acids (RNA and DNA) are examples of biopolymers.

Synthetic polymers: These polymers are made from smaller molecules by chemical means. They are man-made. The raw materials for their preparation are obtained from petroleum and coal tar. Some typical examples of synthetic polymers are polyethylene, synthetic rubber, terylene, teflon, bakelite, etc.

10.2 PLASTICS AND ELASTOMERS

Plastics are those high molecular weight compounds which under the influence of heat and pressure can be molded into tough and hard utility

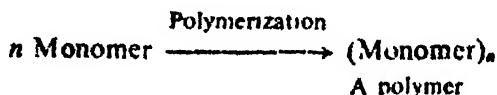
articles. Most of the polymers such as polyethylene, P.V.C., polystyrene, nylon are plastics. Unlike synthetic rubber, plastics show no elasticity at ordinary temperatures. Plastics are light, strong and resist the action of chemicals. The high molecular weight polymers of substances often containing olefinic bonds are most familiar plastics.

Elastomers. Elastomers are those polymers which on vulcanization convert into rubbery products, exhibit good strength and elongation. Typical examples are synthetic and silicon rubber.

Plasticizers. Plasticizers are substances which can impart plasticity to a polymer, i.e., facilitate the conversion of solid and brittle resins into a dough-like condition so that it can be molded into a desired shape. Esters of phthalic acid such as dimethyl phthalate is usually used as a plasticizer. It is added, for instance, to hard polyvinyl chloride (PVC) to soften it.

10.3 POLYMERIZATION

If two identical molecules combine chemically a dimer is obtained. Acetylene, for instance, is dimerized to vinylacetylene. If smaller molecules of a substance unite then a large molecule, a polymer, of high molecular weight is obtained. The chemical process for the formation, of a polymer is called *polymerization*. This is exemplified in the following equation.



Polymerization can be initiated by several processes namely free radical, cationic and anionic. The repeating atomic grouping in a polymer each of which is monomeric in character is termed a *repeat unit*. Another important term is the *degree of polymerization* which refers to the number of repeat units in the polymer and is denoted by n .

A polymer is of two types, i.e., addition and condensation. In *addition polymers*, monomers link together and produce no other molecule in the process. In the case of *condensation polymers*, a small molecule such as H_2O , CH_3OH is eliminated during polymerization.

A synthetic polymer can be linear, branched or cross-linked. The first two kinds are called *thermoplastic* as they dissolve in solvents, soften on heating and can be moulded. Polyethylene is a linear polymer and graft polymers are branched. In a *cross-linked polymer*, the chains are connected to each other by occasional bridges by the addition of chemicals. These polymers generally extend in space in all directions and are, therefore, often called *three-dimensional* net work. They are *thermoset* polymers as they melt on heating and then harden irreversibly as a result of a chemical change. Typical examples of thermoset polymers are bakelite, urea-formaldehyde resins, glyptol, epoxy resins, etc. Thermosetting plastics are

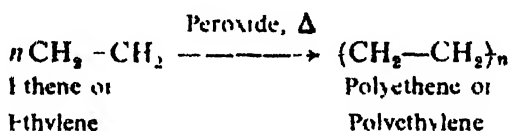
used for making articles which would not soften when heated. Such applications include electrical fittings, saucepan handles and bench tops.

10.4 ADDITION POLYMERS

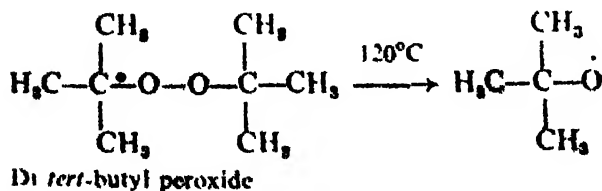
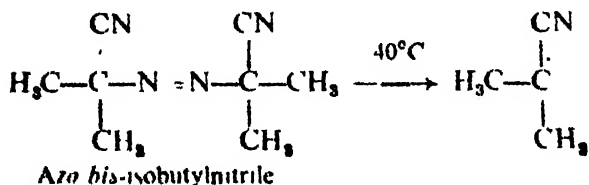
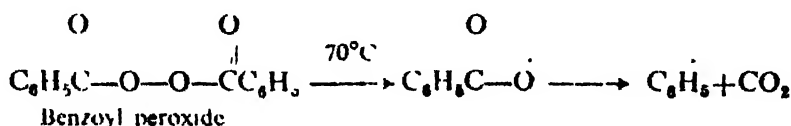
Polymerization of compounds containing double bonds results in the formation of addition polymers. In these polymers self-addition of monomer molecules to each other to form a long linear takes place. The reaction is promoted by free radical initiators and the mechanism of polymerization consists of three steps namely initiation, propagation and termination. The reaction is referred to as *chain polymerization*. In the following pages several examples of addition polymers will be discussed.

10.4.1 Polyethylene

Ethylene is a gas but condenses to a liquid at -103.17°C and solidifies at -169.2°C . It is commercially obtained by cracking of petroleum fraction. Polyethylene can be made under high pressure (1000 atm) and temperature ($180-250^{\circ}$) in the presence of peroxide as a catalyst. The product has low density and low melting point. High density polyethylene is made at low pressure (5-25 atm) and temperature ($20-50^{\circ}\text{C}$) in the presence of Ziegler-Natta catalyst.

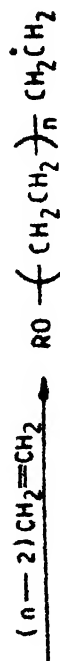
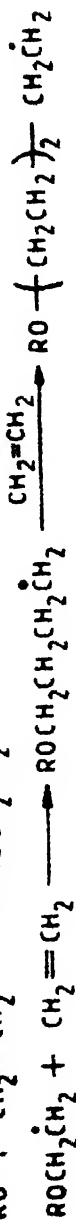


The mechanism of this reaction is brought about by free radicals produced by the decomposition of compounds called *initiators*. Some typical free radical initiators and the free radicals formed by their decomposition are listed below:

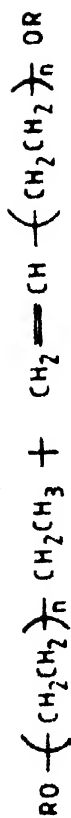
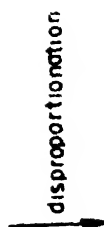
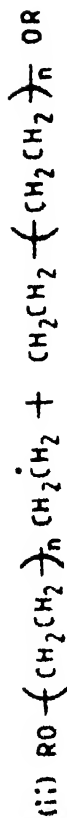
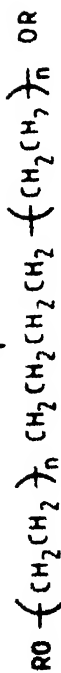


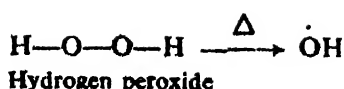


Initiation $\text{R}-\text{O}-\text{O}-\text{R} \longrightarrow 2 \text{RO}^\bullet$



Termination (i) $\text{RO}-(\text{CH}_2\text{CH}_2)_n-\text{CH}_2\dot{\text{C}}\text{H}_2 + \dot{\text{C}}\text{H}_2\text{CH}_2-(\text{CH}_2\text{CH}_2)_n-\text{OR}$





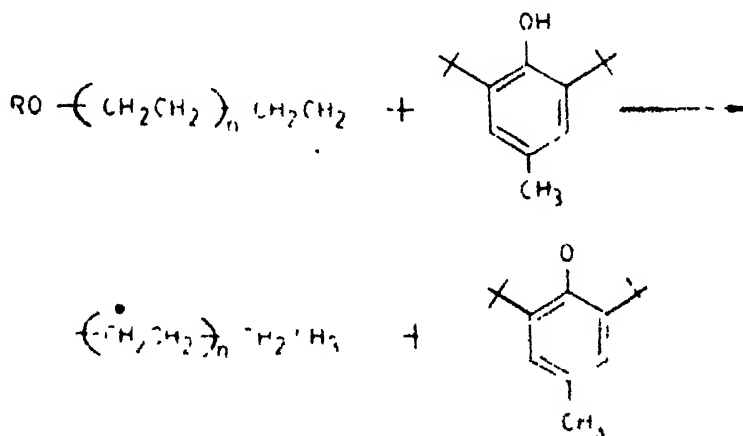
The different steps in the mechanism may be formulated as on page 210. Ethylene is heated in the presence of a peroxide, benzoyl peroxide is the most common one. Thermal decomposition of peroxide produces free radicals (OR^\bullet). A free radical being very reactive attacks an olefin molecule and in the process generates a new free radical. In the propagation step this radical attacks the double bond of a fresh olefin and thus links another molecule with it. This chain contains a radical site, therefore, it attacks yet another olefin. This process continues and the chain keeps growing till all the olefin is consumed, or the chain growth is stopped by termination. The last step is the termination step, i.e., in which the reaction is terminated. In this step two large growing chains come close and couple together to stop this reaction, this is called *coupling*. Alternatively one hydrogen atom from one chain is abstracted by the second chain and thus both stabilize themselves. The chain losing a H stabilizes itself by the formation of a double bond. This process is called *disproportionation*.

At this point it is important to note that most polymers are not pure but are complex mixtures of compounds. We often determine the average molecular weight of the polymer with an average value n , for the mixture.

Low density polyethylene is extremely flexible and water resistant and is used in packaging and for making plastic bags, toys and artificial flowers. High density polyethylene is stiff and is employed in making house-hold goods such as pails, refrigerator dishes and kitchen wares.

10.4.2 Free Radical Inhibitors

Certain chemical compounds which are capable of inhibiting or completely stopping the chain growth process called *radical inhibitors*. Phenolic compounds are very useful for this purpose as the phenolic hydrogen is easily

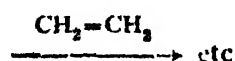
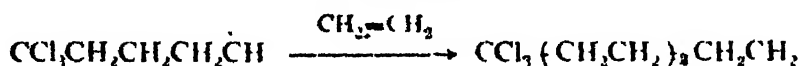
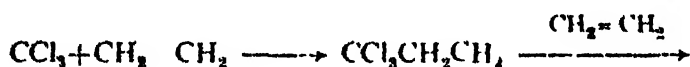
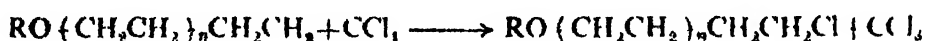


abstracted by the polymer chain, and thus converting them into stable free radicals. This is exemplified by the accompanying reaction:

The phenoxy radical is stabilized by the steric effects of the bulky *t*-butyl groups of 2, 6-di *t*-butyl-4-methylphenol and no further reaction is possible. Besides terminating polymer chains, inhibitors are used in the preservation of monomers during production and storage. Hydroquinone is often added to monomers to prevent their polymerization.

10.4.3. Chain Transfer

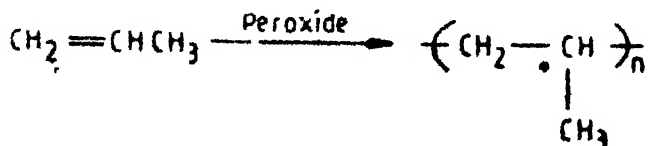
A polymer chain, as has been discussed, may be terminated by coupling, disproportionation or the addition of radical inhibitors. There is yet another way of doing this by chain transfer reactions. In the earlier methods the products formed were *inactive* and further chain propagation was not possible. In *chain transfer* reactions, on the other hand, while the growth of one chain is stopped completely there is a simultaneous initiation of a new polymer chain. A compound that brings about chain transfer is called a *chain transfer agent*, such as carbon tetrachloride, thioalcohols and toluene. The chain transfer reaction starts by removal of a hydrogen or some other atom by the polymer chain from the chain transfer agent as indicated below.



The initial polymer chain is now terminated but the new radical $\text{CCl}_3\cdot$ adds to a fresh ethylene molecule. A new radical is again generated which is followed by the propagation step. It is obvious that one chain is transferred to another chain and hence the name *chain transfer*. This type of reaction is used to regulate the molecular weight of polymers.

10.4.4 Polypropylene

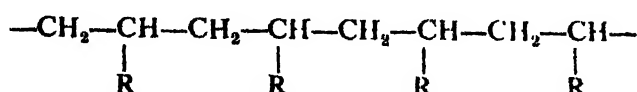
Propylene is a gas, m.p. -185.2°C and is obtained by the cracking of petroleum products. It can be polymerized in the presence of peroxides or Ziegler-Natta catalyst (Triethyl aluminum and titanium chloride).



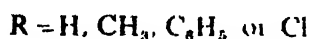
Polypropylene

Polypropylene is tougher than polyethylene. It is used for making ropes, for making plastic goods and in packaging.

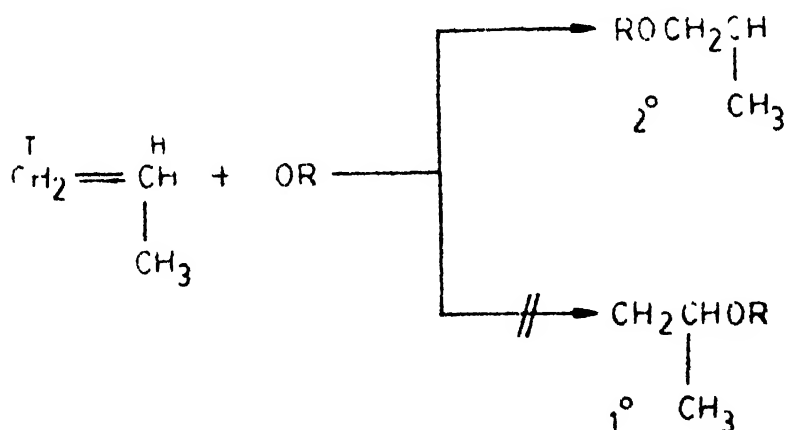
The polymer chain in a free radical process is made up of the repeat units and could be very large. The polymer would have the following regular form:



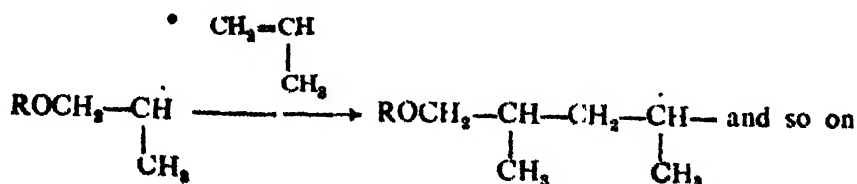
where



In ethylene, a symmetrical olefin, the monomer can attach on either side to form polyethylene. Propylene is an unsymmetrical olefin and the question of attachment of the second propylene molecule arises. An examination of the above general structure reveals that polymerization takes place in a head-to-tail manner, $-\text{CH}-$ being the head and $-\text{CH}_2-$ the tail. How do we account for this? Let us consider the formation of the intermediate radical when OR^\bullet adds to propylene.



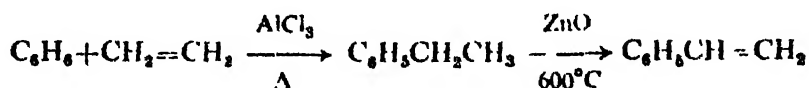
Obviously two radicals are formed depending on the attack of OR^\bullet at the two carbon atoms linked by a double bond. Out of the two radicals the former is more stable being secondary. Therefore, this will control the propagation step. Its formation is also favored by the fact that attack of OR^\bullet at the internal carbon will be sterically hindered. The secondary radical will attack another propylene molecule generating a new radical.



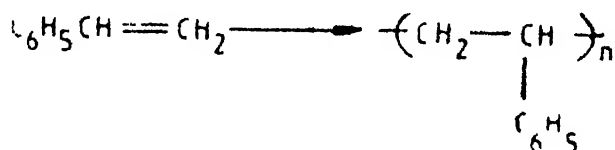
The process will continue. The growing polymer chain would thus be joined in a head-to-tail manner.

10.4.5 Polystyrene

Styrene is a liquid with a pleasant odor, b.p. 45°C . It is obtained by the Friedel-Crafts reaction between benzene and ethylene.



Styrene so obtained is purified by distillation. It is polymerized industrially by the free radical procedure. It being an unsymmetrical olefin, the polymerization occurs in a head-to-tail manner.

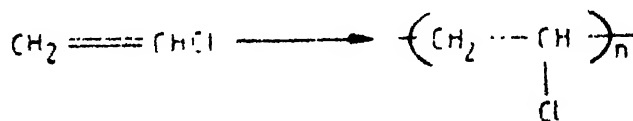


Polystyrene (Styrofoam)

Polystyrene is thermoplastic and has good electrical insulating properties. It is chemically inert and is used for making toys, jars, radio and television cabinets and other household goods. Copolymerization of styrene with 1, 3-butadiene yields synthetic rubber.

10.4.6 Polyvinyl Chloride

Vinyl chloride is a gas, b.p. -13°C . It polymerizes readily in the presence of peroxides or heat.

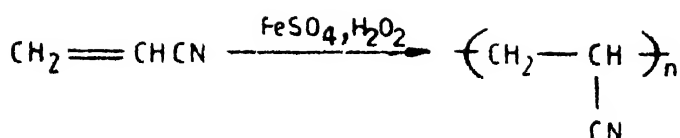


Polyvinyl Chloride (PVC)

PVC is a white amorphous powder. It is cheap and commercially available. It is tough and is used as building material. With added plasticizers to soften it, is used in making upholstery, pipes, curtains and rain coats.

10.4.7 Polyacrylonitrile

It is obtained by polymerizing acrylonitrile using peroxide radical initiators

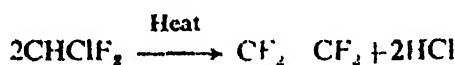
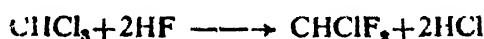


Polyacrylonitrile (PAN)

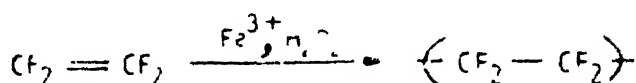
Polyacrylonitrile fibres are marketed under such trade names as *Acrilan*, *Orlon* or *Dralon*. It offers excellent resistance against heat. The fibre is used for making carpets, pipes and blankets. PAN copolymerizes with 1, 3-butadiene to form synthetic rubber.

10.4.8 Polytetrafluoroethylene

The monomer tetrafluoroethylene is a gas, b.p. -76°C . It is obtained in the following manner by the pyrolysis of chlorodifluoromethane.



Polymerization of this alkene was an accidental discovery.



Polytetrafluoroethylene (PTFE)

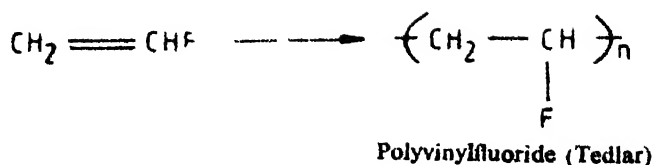
This polymer is commercially known as *Teflon*, and has a high melting point (327°C). It has a low coefficient of friction and is used for coating surfaces to reduce friction. Teflon also is highly resistant to the action of heat and chemicals. For this reason it is used for coating non-stick frying pans, for making gaskets and valve seals.

10.4.9 Polyvinylfluoride

Vinylfluoride is a gas, b.p. -72°C and is obtained by the addition of HF to acetylene.



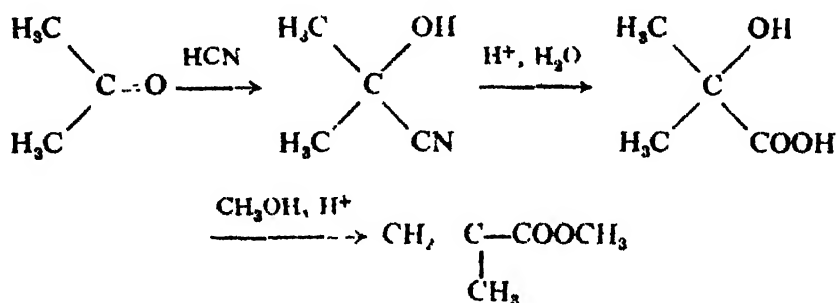
It is polymerized at 85°C in the presence of benzoyl peroxide.



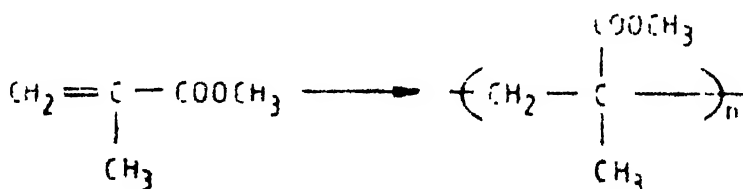
This polymer is known as *Tedlar*. It is a crystalline polymer, m.p. 200°C . It is widely employed as an excellent weather proofing coating, and in the building industry.

10.4.10 Polymethylmethacrylate

The monomer methyl methacrylate is obtained from acetone according to the following sequence of reactions.



Polymethylmethacrylate is obtained by radical polymerization of the monomer.

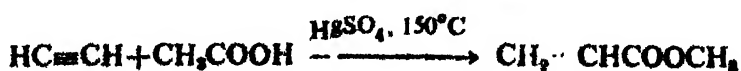


Polymethylmethacrylate (Plexiglas)

It is popularly known as *Plexiglas* or *Lucite*. It is a colorless transparent plastic and has excellent optical properties, and is a substitute for glass. It is used in making attractive sign-boards and long-lasting lenses for automobile lights.

10.4.11 Polyvinyl Acetate

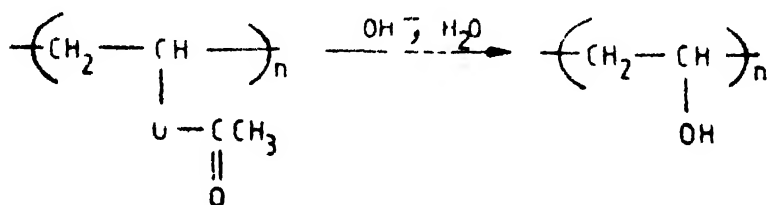
Vinyl acetate is prepared by a gaseous phase reaction between acetylene and acetic acid. It is then polymerized by radical process.





Polyvinyl acetate (PVA)

It is soluble in organic solvents and is employed extensively in emulsion paints and as adhesives. It is also used for the preparation of polyvinyl alcohol. Polyvinyl alcohol is prepared indirectly by the hydrolysis of polyvinyl acetate.

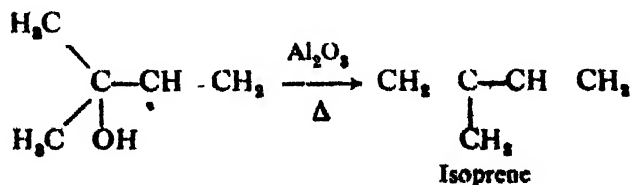
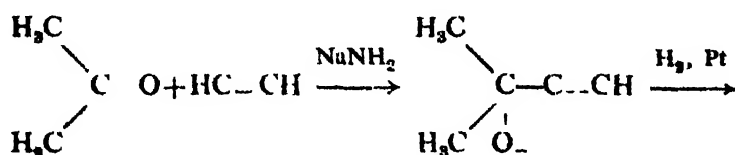


Polyvinyl alcohol

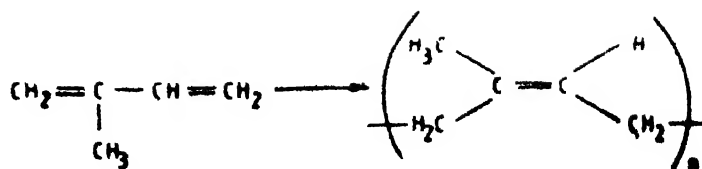
Unlike many polymers, polyvinyl alcohol is soluble in water. It finds use in adhesives and in the manufacture of textile fibres.

10.4.12 Natural Rubber (Polyisoprene)

Natural rubber is a mixture of hydrocarbons having the empirical formula C_5H_8 . It is highly unsaturated and a careful ozonolysis establishes that it is a linear polymer of isoprene (2-methyl-1,3-butadiene). Isoprene may be prepared by the condensation of acetone and acetylene in the presence of a strong base.

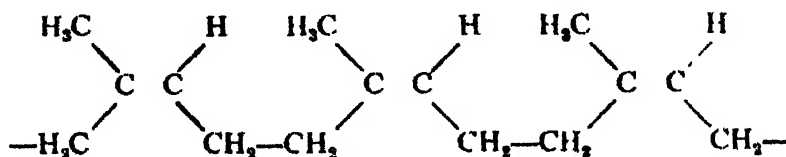


Isoprene polymerizes to a product identical with natural rubber.



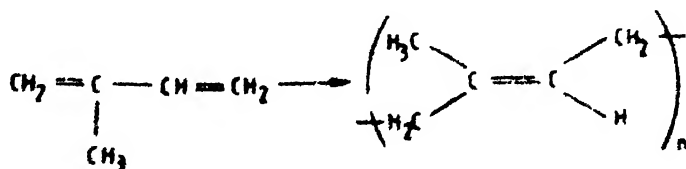
Polyisoprene

Natural rubber is a large molecule composed of about 4500 isoprene units. It is a linear polymer and the isoprene units are linked in a head-to-tail manner. The olefinic linkages are all in *cis*-configuration. A segment of natural rubber is shown below :

*cis*-Polyisoprene (natural rubber)

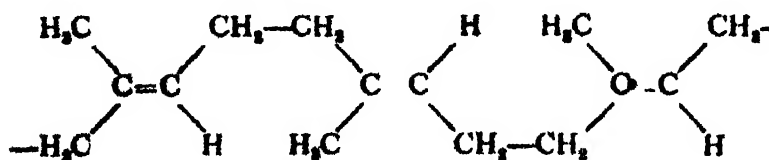
In natural rubber there is free rotation about the C—C bond which gives it some flexibility. It is used in a wide range of applications including automobile tyres.

The *trans*-isomer of natural rubber is called *gutta percha*. It is also built of isoprene units. It is obtained by the evaporation to dryness of the sap of tropical *plaguim* trees.



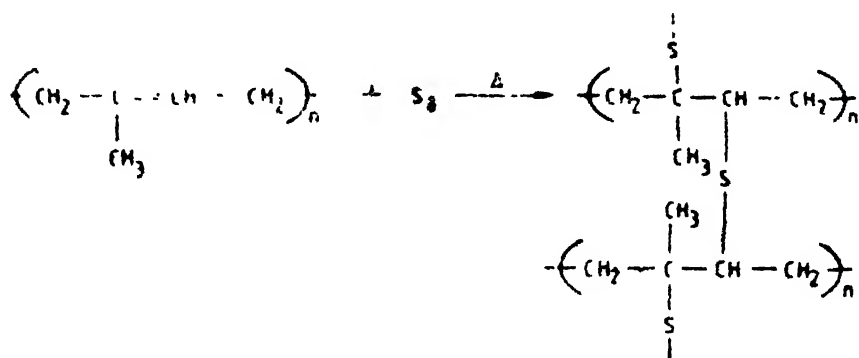
Gutta percha

A segment of gutta percha is shown below:

*trans*-Polyisoprene (gutta percha)

Gutta percha is a horny rather than elastic. It is tough and hard and is used in a limited range of applications such as golf ball covers and as an insulating material in submarine cables.

Natural rubber is obtained in the form of *latex* or milky sap, a colloidal solution of rubber in water from a tree (*Hevea brasiliensis*). The sap contains natural products such as resins, sugars, fatty acids besides rubber. The rubber content varies from 30% to 50%. The latex is placed in large vats and coagulated by the addition of 1% acetic acid. This gives *gum rubber*. This rubber does not have high tensile strength and becomes brittle at low temperatures. Because of this property very little use of rubber was made before the discovery of vulcanization by Charles Goodyear in 1839. According to this sulfur is added to affect cross-linking between linear polymer chains.

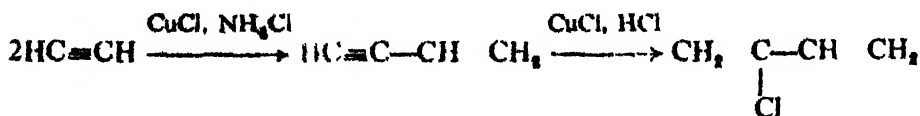


The resulting rigid structure obtained is described as a cross linked thermoset polymer. The properties of natural rubber are changed remarkably and it can be usefully employed for industrial applications. Vulcanized rubber is used for making gloves, rubber bands, tubes and in automobile industry. The property of rubber can further be modified by the addition of antioxidants (diphenylamine) to protect rubber from deterioration on exposure to air.

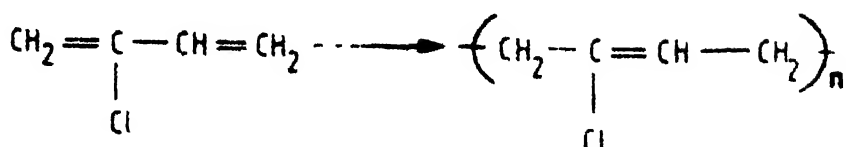
Soft rubber contains about 1-2% sulfur while *hard rubber* contains upto 35% sulfur and is not elastic any more.

10.4.13 Neoprene (Synthetic Rubber)

This was the first synthetic rubber made in America. For its preparation the monomer chloroprene (2-chloro-1, 3-butadiene) is obtained from acetylenic,

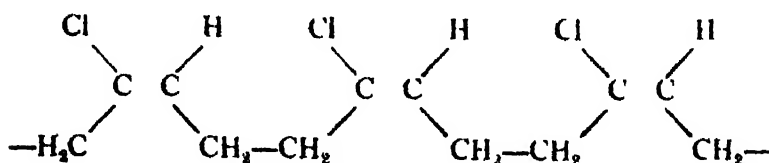


Chloroprene is then polymerized to neoprene.



Polychloroprene (Neoprene)

In neoprene the methyl groups of natural rubber are replaced by chlorine atoms. The configuration of the groups around the double bond is *cis*.

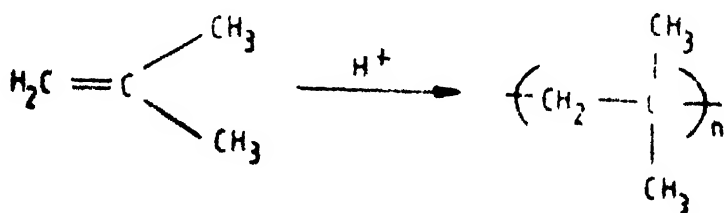


cis-Polychloroprene (Neoprene)

Neoprene is non-inflammable. It is resistant to the action of oils, petrol, grease and lubricants. It is, therefore, used in making delivery hoses for petrol and for making industrial conveyors and belts.

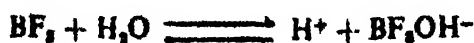
10.4.14 Polyisobutylene

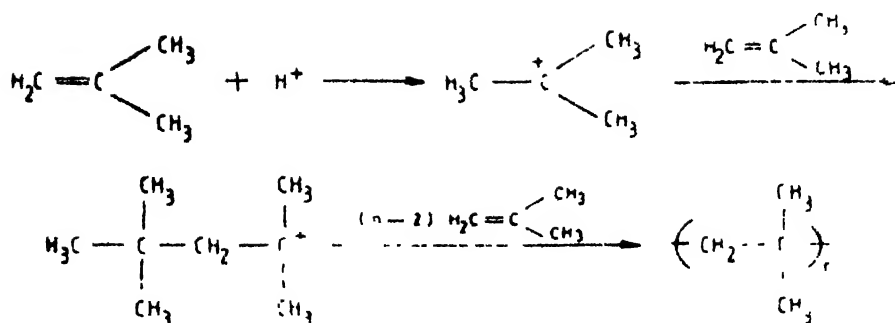
Iso-Butylene is a colorless gas and is also obtained from petroleum. It polymerizes in the presence of acids and the growing chain in this case is cationic rather than free radical.



Polyisobutylene

The mechanism for its formation can be formulated as follows.



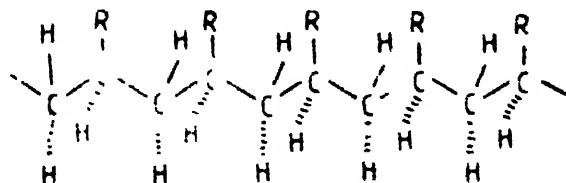


Polyisobutylene

Polymerization is initiated by the donation of a proton from an acid (a Lewis acid BF_3 containing a few drops of water) to isobutylene. A tertiary carbocation is formed. Propagation takes place through the repeated addition of the monomer molecules to the carbocation. A linear polymer is obtained by head to-tail addition. Ethylene is not polymerized by cationic process because it does not have alkyl groups to sufficiently stabilize the carbocation. Polyisobutylene is water and chemical repellent and is employed as a corrosive resistant and protective film. A copolymer of isobutylene with 2-5% isoprene is marketed under the name "*Butyl rubber*". It is used in making cycle and automobile tubes.

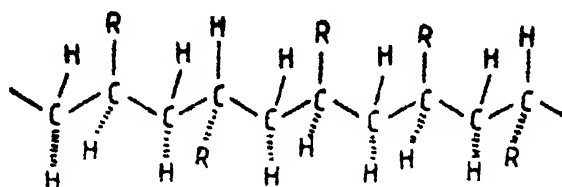
10.5 ORIENTATION IN POLYMERS

In a polymer made up of long chain-like molecules, molecular motion is curtailed and rotation even around single bonds is restricted. As a result head-to-tail polymers can have varying orientation of the side groups which can be in either orderly or disorderly fashion with respect to the chain. These different arrangements are isotactic, syndiotactic and atactic and are shown for propylene. In *isotactic* (for *cis* arrangement) all the methyl groups lie on one side of the chain and the hydrogen atoms on the other.



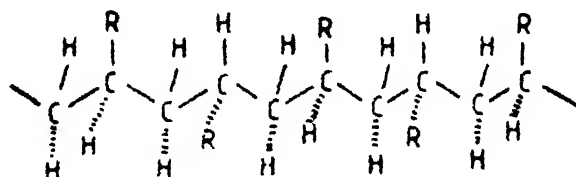
An example of this class of arrangement is natural rubber. Isotactic polymers have a high degree of crystallinity and are prepared by the use of Ziegler Natta catalyst.

If the methyl and hydrogen atoms fall alternately above and below the chain, then this orientation is referred to as *syndiotactic* (for a *trans* or alternating arrangement).



Gutta percha is an example of this type of arrangement.

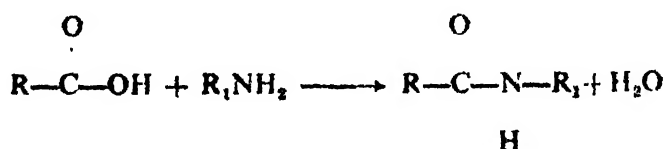
The third type *atactic* (Greek without order) is used for the random arrangement of groups above and below the chain.



This type of polymer is obtained by free radical polymerization

10.6 CONDENSATION POLYMERS

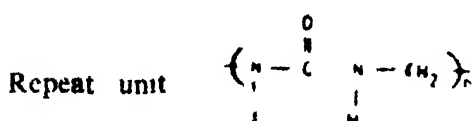
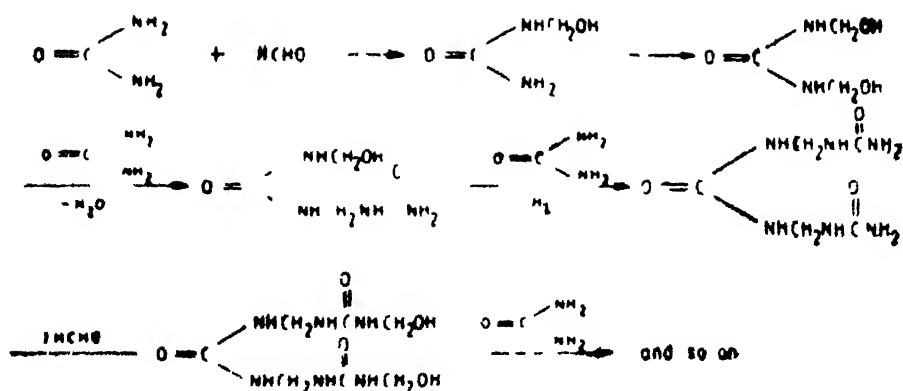
In a condensation polymer two organic reagents combine with the elimination of smaller molecules. A well known example is the linking of an amine to a carboxylic acid to yield an amide.



Polymers can be synthesized through this reaction by using a mixture of dicarboxylic acids and diamines. With these types of reagents this method leaves a free acid function at one end and an amine at the other so that polymerization can continue indefinitely. In condensation polymers also the polymer molecule contains a structural identity repeating itself several times but less number of atoms are present than in the monomers of the repeat unit.

10.6.1 Urea-Formaldehyde Resins

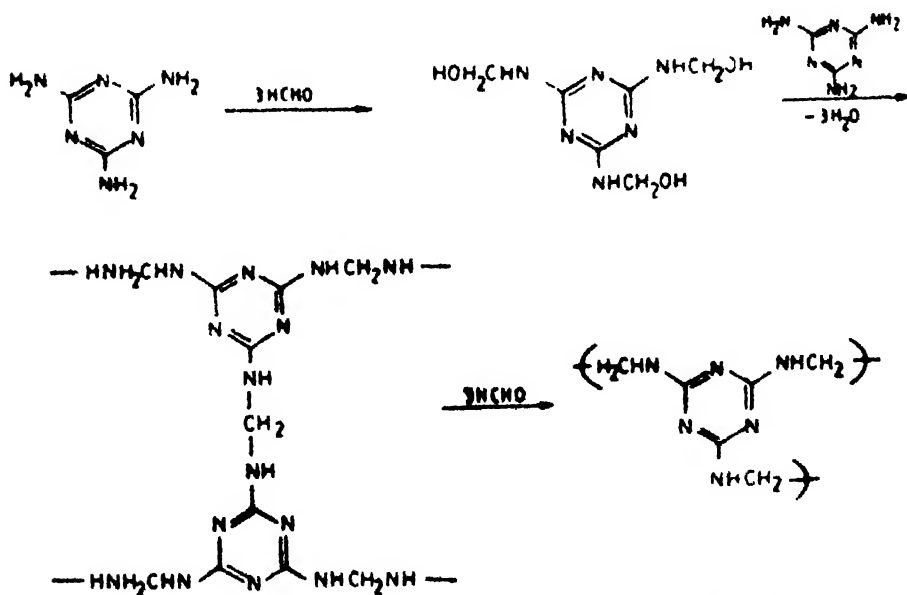
Urea condenses with formaldehyde to form urea-formaldehyde resin.



This resin is inert towards the action of chemicals and is used as adhesive in industry

10 6 2 Melamine Polymer (Melmac)

This polymer is prepared from melamine—formaldehyde reaction.



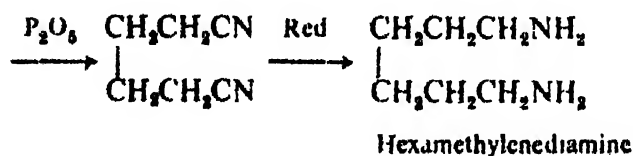
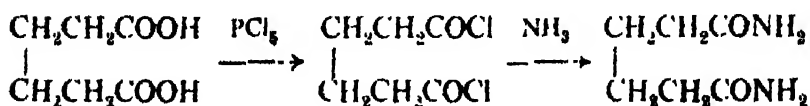
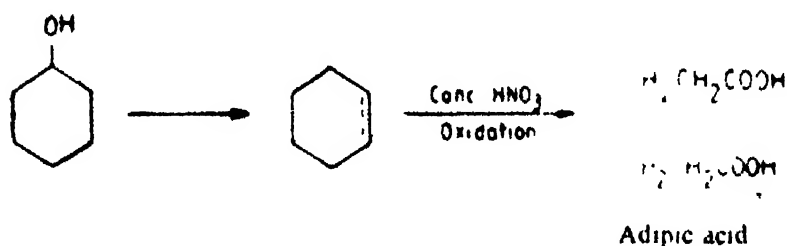
Melmac

It is a three-dimensional net-work polymer. Melmac has better heat and water resistance properties and is employed in making household crockery.

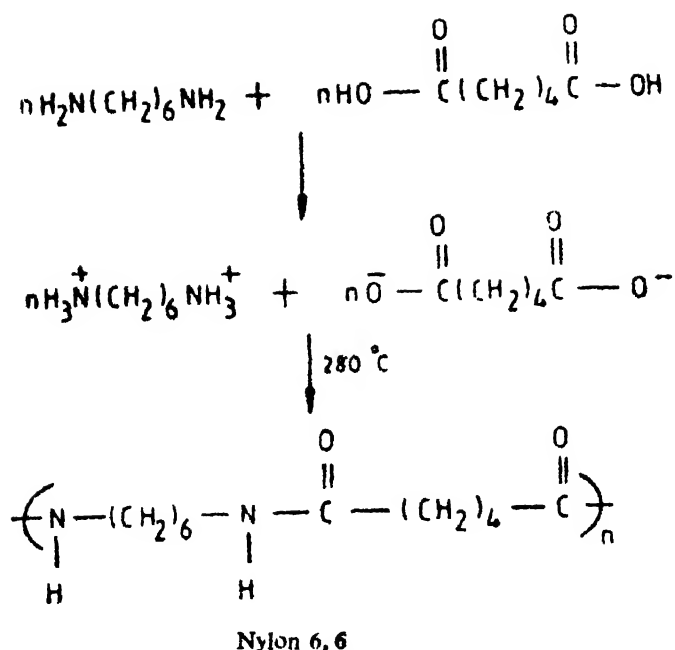
10.6.3 Nylon 6, 6

The aliphatic polyamides are generally known as nylons. The $\begin{array}{c} \text{O} \\ | \\ -\text{N}-\text{C}- \\ | \\ \text{H} \end{array}$

segments are amide groups so this is why nylon is considered to be a member of the family of materials termed as *polyamides*. There are different types of nylon and they are named by a numbering system. The number indicates the number of carbon atoms present in the monomer. Nylons are obtained by condensation reactions, and are thus classified as condensation polymers. Nylon 6, 6 is obtained by condensing hexamethylenediamine with adipic acid. The monomers are prepared as follows:



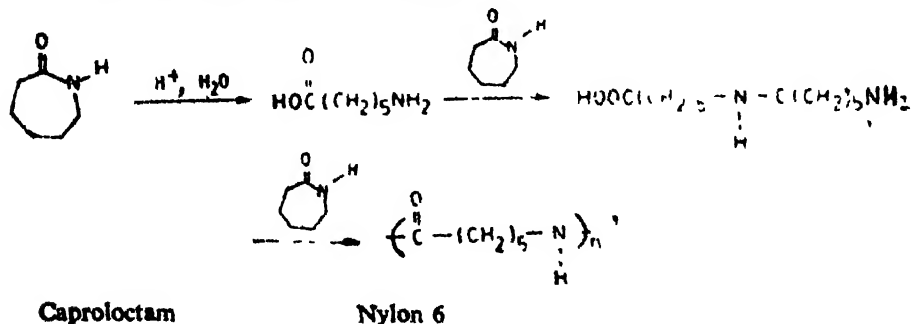
Nylon 6, 6 is obtained on heating a mixture of the monomers at 280°C.



Both in Nylon 6, 6 and Nylon 6, the molecular chains are held together by intermolecular hydrogen bonding between >C=O and $-\text{N}-\text{H}$ groups of the adjacent chain. Nylon 6, 6 is used as plastic and a fibre. It is very hard and also has a good tensile strength. It does not absorb moisture and is not attacked by moth. It is used in making tyre cord, fishing nets, strings for musical instruments and in the textile industry.

10.6.4 Nylon 6

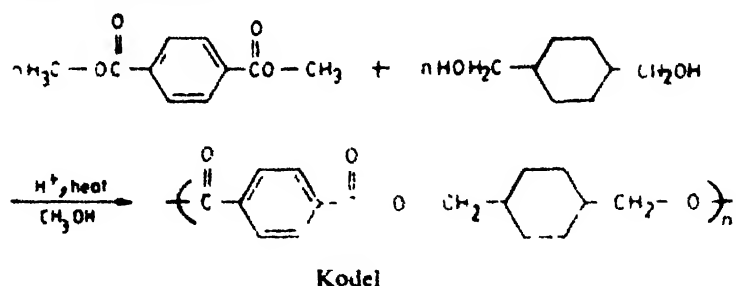
Nylon 6 is obtained from caprolactam. The monomer may be obtained from cyclohexanone *via* the Beckmann rearrangement. Caprolactam contains a seven membered ring and can be easily opened in the presence of acids. Polymerization takes place on heating.



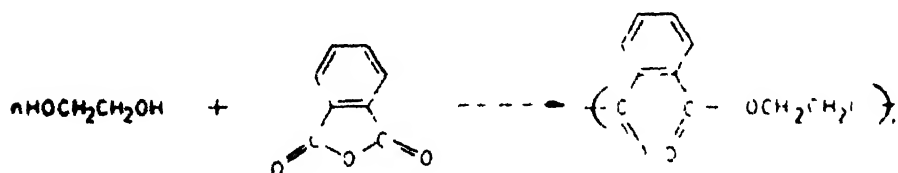
Nylon 6 is fabricated into sheets and used in tyre industry. It is a polymer of great importance in synthetic fibre industry.

10.6.5 Kodel

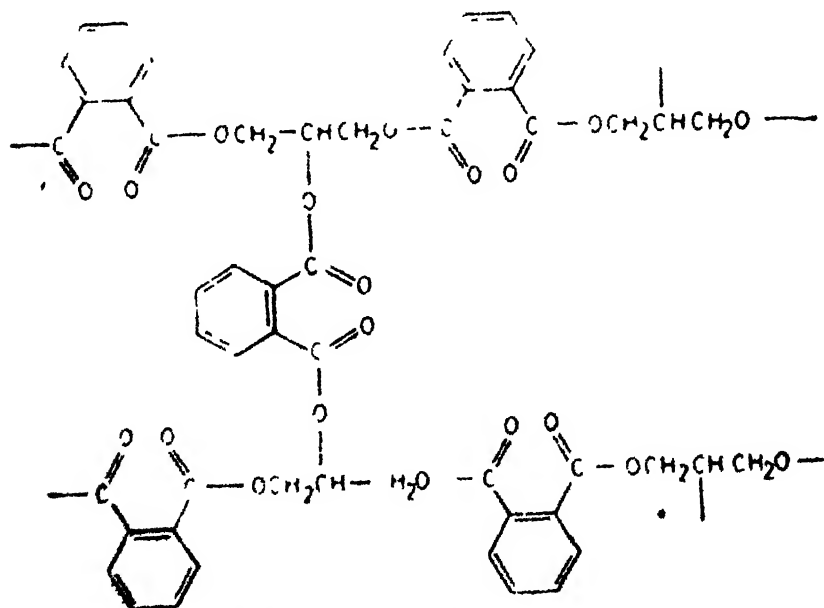
It is a polyester and is prepared by condensing dimethyl terephthalate and 1,4-cyclohexan dimethanol.

**10.6.6 Glyptal Resins**

A dialcohol and a dicarboxylic acid form a linear polymer. For instance, glycol with phthalic anhydride yields polyethylene phthalate



A trihydroxy alcohol, on the other hand, forms a net work polymer. A typical example is the glyptal resin, produced from glycerol and phthalic anhydride.



This polymer is used as an ingredient of paints and varnishes.

10.6.7 Thiokol Rubber

Thiokol was the first synthetic rubber made. It is called *Thiokol* in U.S.A. and *Perdurene* in Germany. It is a condensation polymer of 1,2-dichloroethane and sodium polysulfide (Na_2S_x).



Thiokol is unaffected by oil, grease or petroleum and is used for making hoses and tank lining. It is unsuitable for making tyres.

10.6.8 Cellophanes

These are made from cellulose dissolved in caustic soda and carbon disulfide. Viscose so formed is given several treatments to obtain cellophane. Cellophanes is unsurpassed in transparency and brilliancy and is extensively used in packaging.

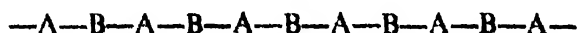
10.7 COPOLYMERS

A polymer made of a single repeat unit is called a *homopolymer* such as polyethylene, polyvinyl chloride or polystyrene. A monomer can also interact with a monomer of a different chemical structure in such a way that both of them are incorporated into the polymer chain. Such a polymer is termed as a *copolymer*. The process by which this is achieved is called *copolymerization*. A copolymer often has better properties than a homopolymer. Copolymers are classified into four types.

Random Copolymers The two monomers (A and B) are arranged in a random manner in the copolymer.



Alternating Copolymers The two monomers are incorporated alternatively along the chain of the copolymer.



Block Copolymers A sequence (or block) of one monomer is followed by a sequence of the other in the copolymer.

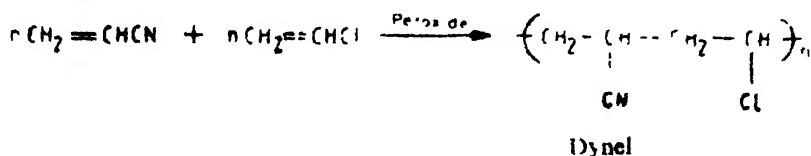


Graft Copolymers These are branched polymers and contain main chain of exclusively one monomer with branches of the second monomer.

The configuration around the C - C is *trans*. This is the best known example of copolymerization in which brittle polystyrene has been made elastic. This is the most important synthetic rubber and a large percentage of tyres today are made of this rubber.

10.7.3 Dynel

It is another example of a copolymer in which two monomers namely acrylonitrile and vinyl chloride copolymerize to yield dynel.

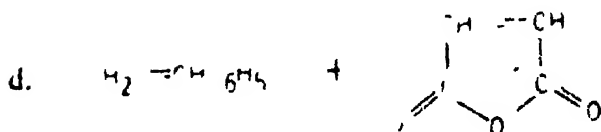
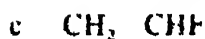
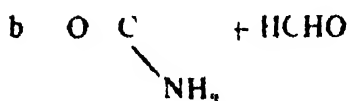
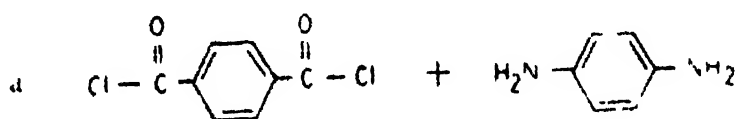


Dynel can be fabricated into fibres that resemble hair.

QUESTIONS

- 10.1 What are addition and condensation polymers? Explain with examples.
- 10.2 Describe the following with a suitable example :
Butyl rubber, gum rubber, soft rubber, synthetic rubber, thiokol rubber, cellophanes.
- 10.3 Account for the fact that radical polymerization of styrene occurs in a head-to-tail manner.
- 10.4 Give the structure of the monomer/monomers from which each of the following is likely to be made.
Plexiglas, orlon, teflon, nylon 6, saran wrap, neoprene, tedlar, styro-foam and Buna-S.
- 10.5 Describe the naturally occurring rubber. What type of polymer is it?
- 10.6 Why is natural rubber vulcanized? Describe the process of vulcanization.
- 10.7 Describe the following briefly with a suitable example :
Plastics, copolymerization, radical inhibitor, monomer, degree of polymerization, branched polymer, chain transfer reactions and polyamide.
- 10.8 Suggest a synthesis for the monomer used for the formation of the following polymers :
Nylon-6, methyl methacrylate, tetrafluoroethylene, acrylonitrile, neoprene and polystyrene.

- 10.9 Describe the purpose of the following compounds in polymer chemistry. Benzoyl peroxide, hydroquinone, carbon tetrachloride, ethyl thiol, hydrogen peroxide.
- 10.10 List three methods of terminating a growing polymer chain with suitable examples
- 10.11 Answer the following and give reasons
- Can ethylene be polymerized by the cationic process?
 - Is polyvinyl alcohol soluble in water?
 - Is natural rubber flexible?
 - Can neoprene be used for making delivery hoses for petrol?
- 10.12 What is a cross-linked polymer? What is the use of cross-linking polymers?
- 10.13 Write the repeat unit of the polymers that would be obtained in the following cases:



- 10.14 Name and write structures of the three modes of orientation of groups in polypropylene. Which of them is prepared by the G. Natta catalyst?
- 10.15 Write short notes on the following.
Gutta percha, Buna-S, chain transfer reaction, thermoplastic and thermoset polymers, graft copolymers and biopolymers.
- 10.16 What are condensation polymers? Describe the synthesis of the monomers used for the preparation of Nylon-6,6. List its industrial applications.

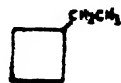
Alicyclic Compounds

Cyclic compounds, made of entirely one type of atoms namely carbon atoms, are known as *carbocyclic* rings. The name *alicyclic* is derived from the fact that they have properties resembling those of corresponding open chain aliphatic compounds. These compounds are represented by the general molecular formula C_nH_{2n} and differ structurally from the open chain compounds in that the terminal carbon atoms are joined by C—C single bonds. These compounds, because of their cyclic nature have an interesting history. Synthetic methods of great value for the preparation of small ring compounds were developed by Perkin (1882-1885). Our knowledge of the chemistry of organic molecules containing small rings has increased tremendously in the last 30 years. Most of the small ring compounds have been found to be very reactive and are stable only under low temperatures while others are postulated as transient intermediates in chemical reactions. Alicyclic

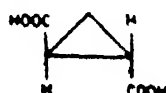
hydrocarbons display both chain isomerism



and



and stereoisomerism, i.e. they can be resolved into optical isomers and exhibit *cis-trans* isomerism as well



cis- and *trans*-Cyclopropanecarboxylic acids



cis- and *trans*-1, 2-Dimethylcyclohexanes

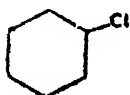
11.1 NOMENCLATURE OF ALICYCLIC COMPOUNDS

Alicyclic compounds are named according to the IUPAC system of nomenclature by attaching the prefix *cyclo* to the name of the corresponding open chain hydrocarbon possessing the same number of carbon atoms. The common names resemble the IUPAC names.

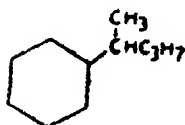
Because there are no ends in a cyclic compound, the carbon atom attached to the substituent gets position 1, and a number to designate its position is not necessary.



Methylcyclobutane

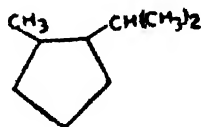


Chlorocyclohexane



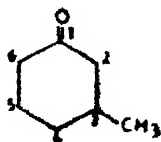
1-Methylbutylcyclohexane

When two or more groups are present, numbering becomes essential.

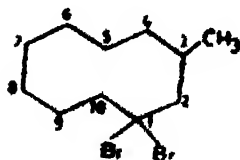


1-Isopropyl-2-methylcyclopentane

The assignment of numbers in a cyclic compound is done in such a manner that the principal functional group is given position 1. Other substituents are given as small a number as possible by going around the ring.



3-Methylcyclohexanone

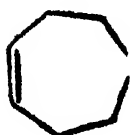


1, 1-Dibromo-3-methylcyclodecane

Unsaturated and unsubstituted cyclic hydrocarbons need no numbering

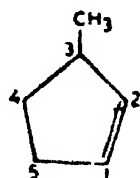


cyclo Butene

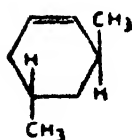


cyclo Heptene

When the principal functional group is olefinic, both the carbon atoms involved in the double bond must be given small numbers. Since the principal group is always numbered 1, there is no necessity to indicate the second

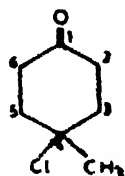


3-Methylcyclopentene

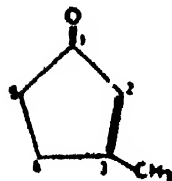


trans-3,5-Dimethylcyclohexene

numeral while writing the name. If two functional groups are present, then the order of preference listed in Table 2.6 (Chapter 2) is followed.

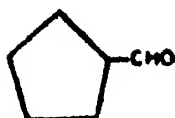


4-Chloro-4-methylcyclohexanone

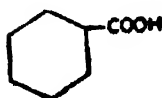


3-Methylcyclopent-2-enone

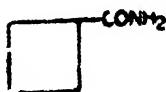
Certain functional groups such as aldehydes, carboxylic acids, amides, esters, nitriles, etc., cannot be included in the basic name of the cyclic portion of the molecule, instead they represent a branch from it. This is illustrated by the following examples:



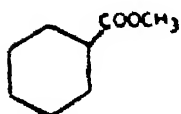
Cyclopentanecarboxyaldehyde



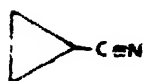
Cyclohexanecarboxylic acid



Cyclobutanecarboxamide



Carbomethoxy cyclohexane

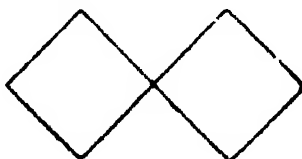


Cyclopropane carbonitrile

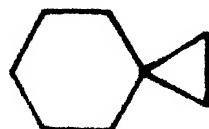
Compounds containing more than one ring and whose ring share two or more of the same carbon atoms are known as *polycyclic compounds*. They are named as follows: A compound containing rings with one common carbon atom is called a *spiran* and is named by using the prefix *spiro* with the name of the parent hydrocarbon. The name of the parent hydrocarbon is obtained by counting the total number of carbon atoms in all the rings. The numbers in the brackets indicate the number of carbon atoms on each side of the common carbon atom.



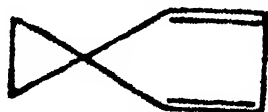
Spiropentane



Spiro [3.3] heptane



Spiro [5.5] octane

Spiro [2.4] hepta-4,6
diene

A compound containing rings with two adjacent carbon atoms in common is called a *condensed ring system*. The word *bicyclo* is prefixed with the name of the parent hydrocarbon. The numbers of carbon atom between bridge-head carbons in the system are indicated by counting from the bridge-head carbon and listing them in a decreasing order within brackets.

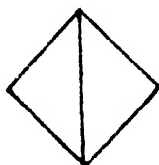


Bicyclo[3.3.0] octane



Bicyclo[4.3.0] nonane

A compound containing more than two atoms in common is called a *bridged* ring system. These compounds are also named as condensed ring systems



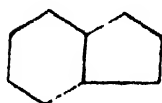
Bicyclo [1.1.0] butane



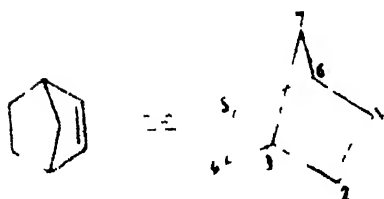
Bicyclo [2.2.0] hexane



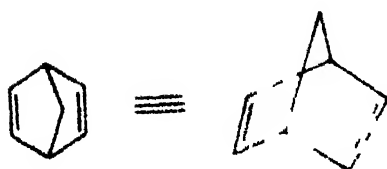
Bicyclo [3.3.0] octane

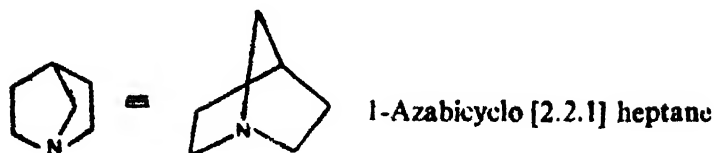
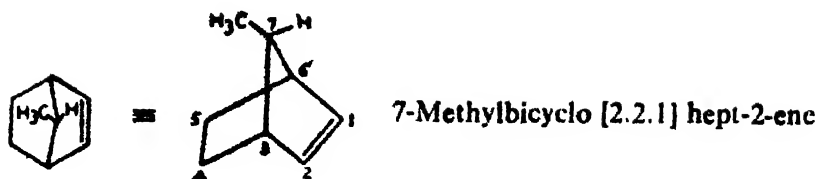


Bicyclo [4.3.0] nonane



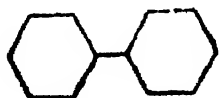
Bicyclo [2.2.1] hept-2-ene (Norbornene)


Bicyclo [2.2.1] hepta-2,5-diene
(Norbornadiene)

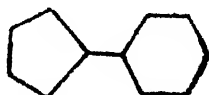


In all the above examples the first two numerals within the parenthesis refer to the number of atoms on both side of the common atoms. The third numeral pertains to the number of common atoms forming the bridge.

A compound joined by a C—C single bond is named simply by using both the ring systems.

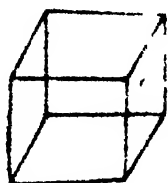


Dicyclohexane

*cyclo* Pentane cyclohexane

Dicyclopentane

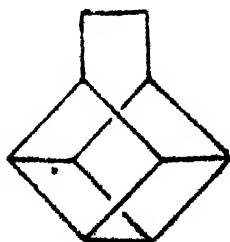
Certain polycyclic hydrocarbons being strained structures are often named on the basis of their shapes.



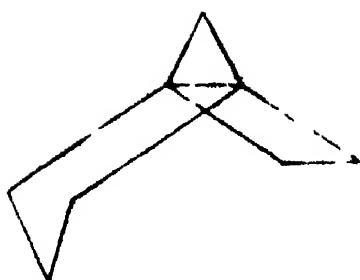
Cubane



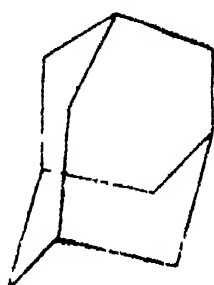
Prismane



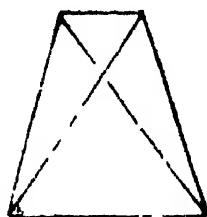
Basketane



Propellane



Admantane



Tetrahedrane

11.2 PHYSICAL PROPERTIES OF ALICYCLIC COMPOUNDS

The boiling points of alicyclic hydrocarbons increase regularly as the ring size increases (Table 11.1), and are 10–20° higher than the corresponding open chain paraffins, e.g.

cyclo Pentane b.p. 49°

n-Pentane b.p. 36°

Like alkanes, cycloalkanes are also non-polar and thus tend to dissolve in solvents like ether, benzene or carbon tetrachloride.

Table 11.1. Physical Constants of Alicyclic Hydrocarbons

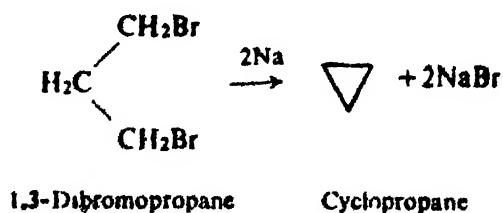
Hydrocarbon	m.p. (°C)	b.p. (°C)
Cyclopropane	-127	-33
Cyclobutane	80	13
Cyclopentane	-94	49
Cyclohexane	6.5	1.8
Cycloheptane	-12	118
Cyclopropene	—	-36
Cyclobutene	—	2.4
Cyclopentene	-93	46
Cyclohexene	-104	83
1,3-Cyclohexadiene	-98	80.5

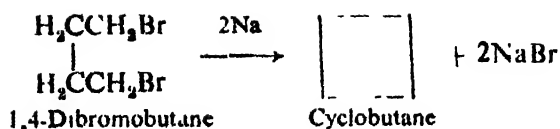
Small ring cycloalkanes are strained ring compounds. A *ring strain* may be described as a strain that gives greater potential energy to certain cycloalkanes. There is an interesting correlation between the thermal stability and the ring size. It is based on the measurement of the heat of combustion, i.e., total amount of heat evolved when one mole of the substance is oxidized to CO_2 and H_2O . As the ring size increases the heat of combustion also increases. Cyclopropane has a value of 499.8 kcal/mole while for cyclohexane it is 944.5 kcal/mole. This implies that cyclopropane has a higher heat of combustion per methylene molecule (app 10 kcal/methylene group more). The cyclopropane ring is thus more strained and its ring strain is estimated at 27.6 kcal/mole while in hexane it is zero.

11.3 GENERAL METHODS FOR THE PREPARATION OF CYCLOALKANES

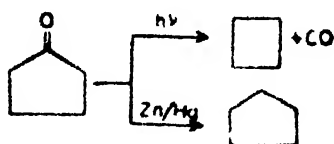
The following general methods may be employed for the preparation of alicyclic compounds and their derivatives

1. An earlier method consists of the action of metallic sodium on ω -dihalogen derivatives

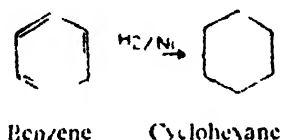




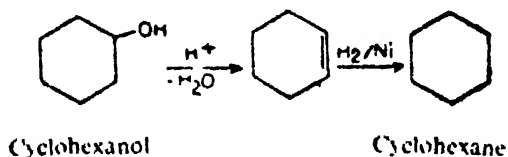
2. Cyclopentanone decarbonylates on photolysis to yield cyclobutane while Clemmensen reduction of cyclopentanone results in cyclopentane formation.



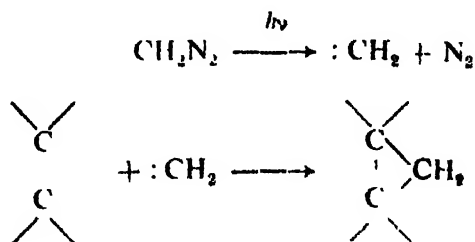
3 Cyclohexane can be obtained by hydrogenation of benzene in the presence of Ni catalyst.



Alternatively it can be obtained from cyclohexanol by dehydration followed by dehydrogenation.

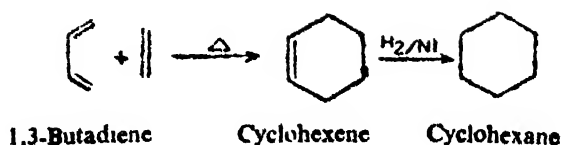


4. An important method for the preparation of cyclopropane is the addition of methylene to C - C bond. The reaction proceeds by the initial

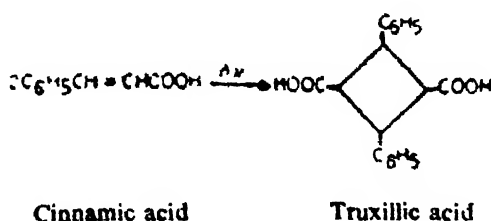


formation of a carbene, the simplest of which is called methylene. Carbenes are neutral divalent species. They react with alkenes by adding to the C - C bond to form cyclopropanes.

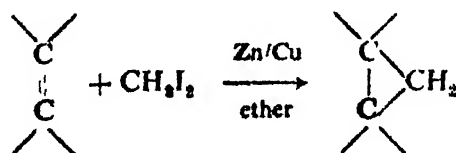
5. The Diels-Alder reaction between 1,3-butadiene and ethylene yields cyclohexene which affords cyclohexane on catalytic hydrogenation.



6. Cinnamic acid on photolysis yields truxillic acid, a cyclobutane derivative.

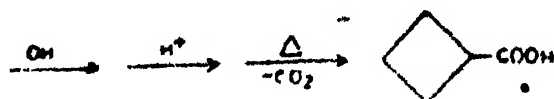
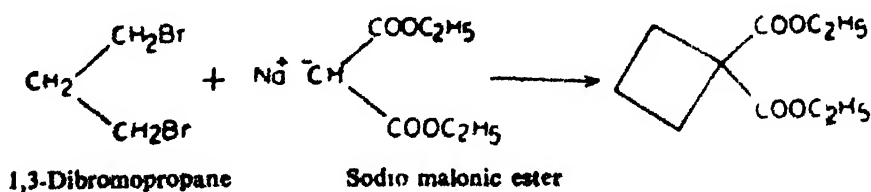


7. **Simmon-Smith Reaction:** Cyclopropane and its derivatives can be prepared by this reaction in which an olefin reacts with CH_2I_2 and a Zn/Cu couple. This reaction also follows a stereospecific *cis* pathway, i.e. a *cis*



olefin yields a *cis* cyclopropane derivative. An organozinc compound is considered the attacking reagent in this reaction.

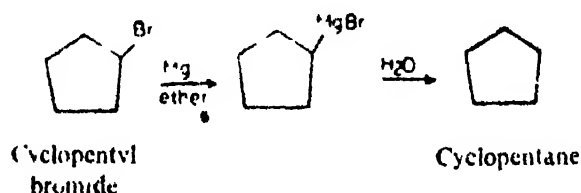
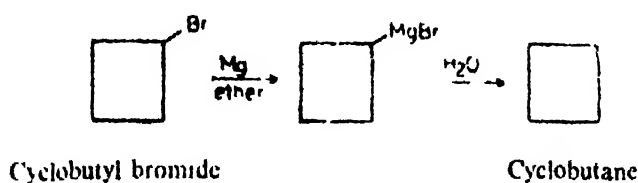
9. An old method for preparing derivatives of four- and five-membered rings is the malonic ester synthesis. Sodium malonic ester is treated with a dihalogen derivative. Subsequent hydrolysis and decarboxylation forms a cyclobutane carboxylic acid.



Cyclobutanecarboxylic acid

Cyclopentane carboxylic acid can be obtained in a similar manner.

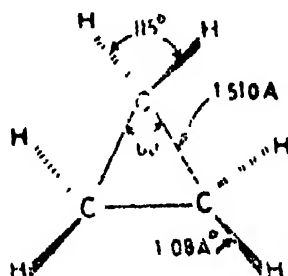
10. *From Grignard Reagents*: All these ring systems can be prepared by treating the corresponding halocycloalkane with a Grignard reagent and then with water.



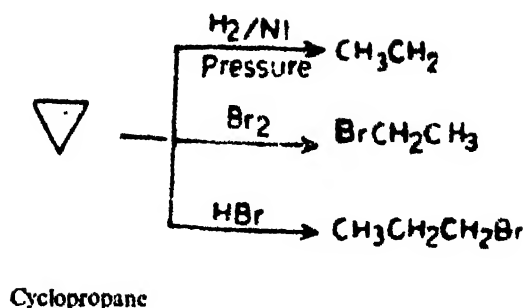
11.4 REACTIONS OF ALICYCLIC COMPOUNDS

The chemical reactivity of each ring system will be considered separately.

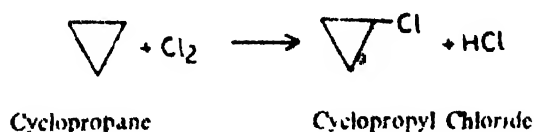
Cyclopropane: Cyclopropane is a planar molecule and has the structure shown below. The internal bond angle is 60° and thus departs from the tetrahedral value of $109^\circ 28'$. This causes angle strain, a strain introduced into



a molecule because of deviation from the tetrahedral angle. A large body of evidence indicates that a cyclopropane ring possesses a double bond character. This suggests that there is more *p*-character in its bonds than in a saturated compound. The most important reaction of cyclopropane is the ring opening with various reagents.



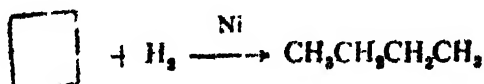
It is chlorinated on photolytic chlorination.



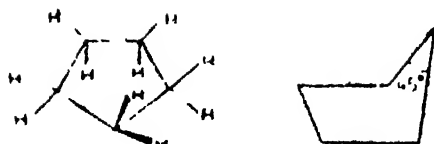
Cyclobutane: This ring is not planar but slightly folded. The ring strain is less severe than in cyclopropane. The internal bond angles are 88°—a



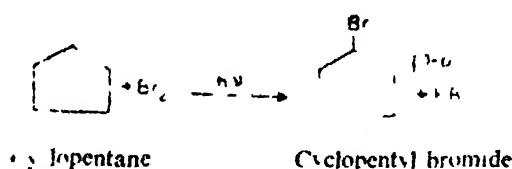
departure of more than 21° from the normal tetrahedral bond angle. It is opened in the presence of hydrogen and Ni. At ordinary temperatures, cyclobutane resists the action of halogens and hydrogen halides.



Cyclopentane: The internal angles of a regular planar pentagon are 108°, a value close to the normal tetrahedral bond angle. Therefore, a planar cyclopentane would be expected to have very little angle strain.



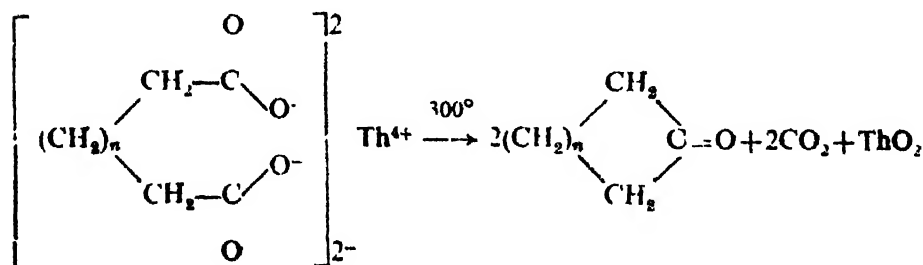
However, in such a structure all of the hydrogens are completely eclipsed. The molecule, thus, attains a slightly bent conformation and the actual structure has the 'envelope' shape. On catalytic hydrogenation, the ring opens to give *n*-pentane. Bromination under free radical conditions yields cyclopentyl bromide.



11.5 LARGE RINGS

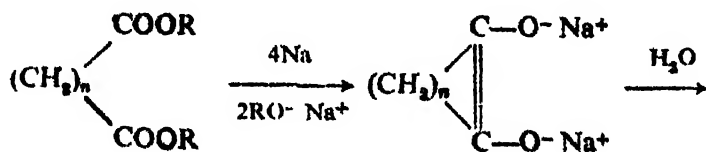
Large ring compounds (higher ketones) were first isolated by Ruzicka from the Himalayan musk deer and the African civet cat. Thus it became clear that large rings can exist. This prompted investigations into their synthesis.

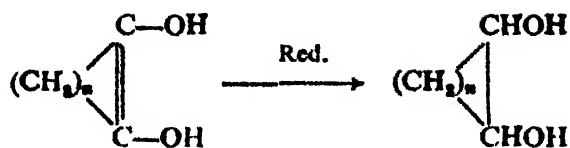
1. Pyrolysis of thorium salts of higher dicarboxylic acids at 300° in vacuum results in ring closure and formation of large ring ketones.



Rings of upto 34 carbon atoms can be obtained.

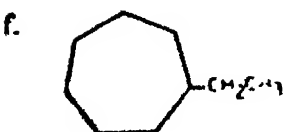
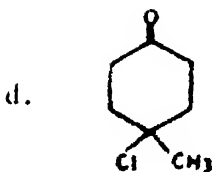
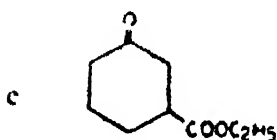
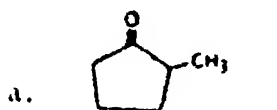
2. Another method consists of treating sodium metal with a higher dicarboxylic acid ester. It forms cyclic acyloins.

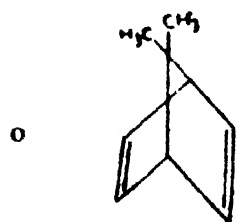
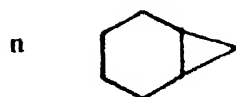
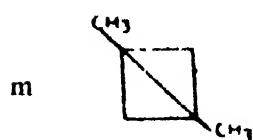
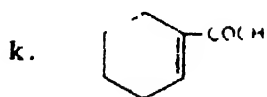
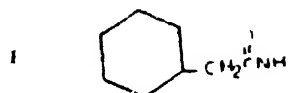
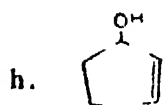


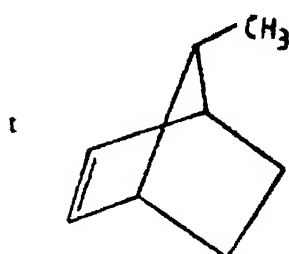
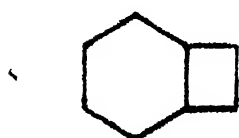


QUESTIONS

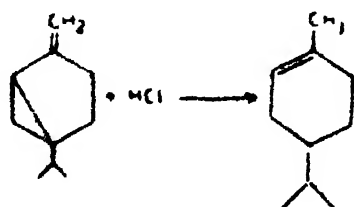
11.1 Suggest IUPAC names for the following structures :







- 11.2 Compare the tetrahedral carbon orbital overlap in ethane with *cyclopropane* and discuss the stability of the two molecules. How has the reactivity of *cyclopropane* been explained on the basis of modern molecular orbital theory?
- 11.3 Describe methods for the preparation of large ring compounds.
- 11.4 Suggest a mechanism for the following reaction



- 11.5 By what means may cyclopropane be prepared?
- 11.6 Describe simple chemical tests to distinguish between the following pairs:
- Cyclobutane* and 1-butene
 - Cyclopentane* and *cyclopentene*
 - Cyclopropane* and Propane
 - Cyclopentane* and 1-pentene
 - Cyclohexane* and benzene

- 11.7 Offer reasons for the fact that 1,2—dibromocyclohexane on treatment with base yields 1,3 *cyclohexadiene* and not *cyclohexyne*.
- 11.8 Why is cyclohexane more resistant to ring opening than cyclopropane?

Aromatic Hydrocarbons

The discussion up to now has been confined mainly to open-chain and cyclic aliphatic hydrocarbons, both saturated and unsaturated. Now we will discuss another most important class of organic compounds—the *aromatic hydrocarbons*. The aromatic compounds are exclusively cyclic and possess a pleasant *aroma*. Coal tar is the principal source of these compounds. They differ from the aliphatic compounds in a number of important ways.

Aromatic compounds are characterized by their cyclic conjugation leading to increased stability. They undergo substitution rather than addition reactions which are characteristic of unsaturated aliphatic compounds, are thermally stable and resistant to oxidizing agents. Kekule was the first to recognize that the early aromatic compounds contain a six-carbon unit and they retain this 'unit' through most chemical transformations. Benzene was eventually recognized as being the parent compound of this series.

12.1 NOMENCLATURE

Benzene is the IUPAC name for the parent aromatic hydrocarbon, C_6H_6 . The names of the substituents located on the benzene ring are derived from the trivial nomenclature. The mono benzene derivatives are thus named systematically by indicating the substituent as a prefix with the word benzene.



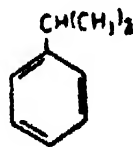
Benzene

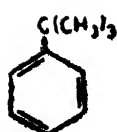
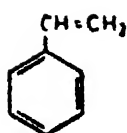


Ethylbenzene

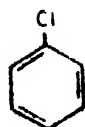


cyclo-Propylbenzene

Iso-Propylbenzene
(Cumene)

*t*-ButylbenzeneVinylbenzene
(Styrene)

Ethynylbenzene



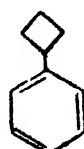
Chlorobenzene



Nitrobenzene



Benzonitrile

*cyclo*-Butylbenzene

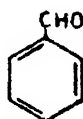
A number of monosubstituted derivatives are given special names and have IUPAC sanction.



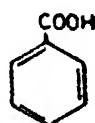
Toluene



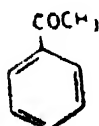
Phenol



Benzaldehyde



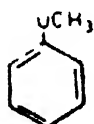
Benzoic acid



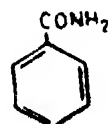
Acetophenone



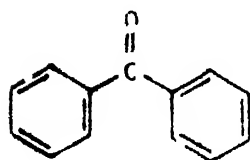
Aniline



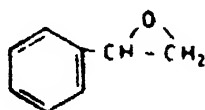
Anisole



Benzamide

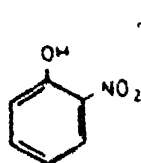


Benzophenone



Styrene oxide

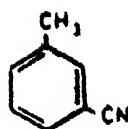
When a second group is introduced on the benzene ring, it may occupy three possible positions giving rise to three isomers. It is possible to number the ring commencing from the group selected as the parent compound. Alternatively, another method is often used in which case the isomers are given names depending on the positions of the substituents; *ortho* (1,2), *meta* (1,3) and *para* (1,4). Thus the names of the derivatives of benzene can be derived from the parent compound.



o-Nitrophenol

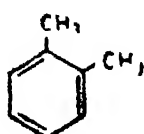


p-Bromoaniline

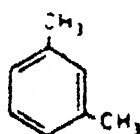


m-Tolunitrile

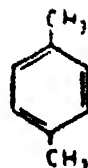
A number of disubstituted derivatives of benzene are also given trivial names that are in common use, such as the following:



o-xylene

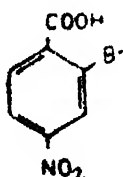
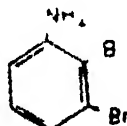
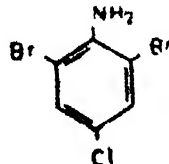


m-xylene

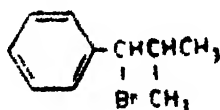
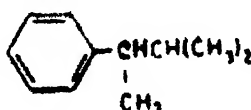


p-xylene

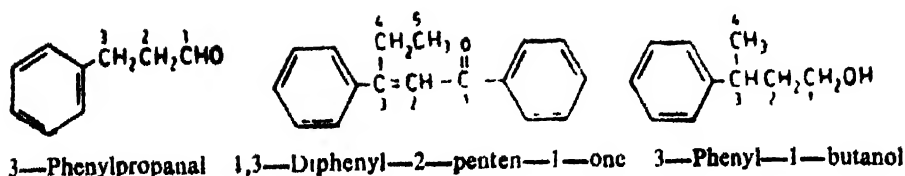
Polysubstituted benzene derivatives are named in a systematic manner by assigning position 1 to the principal functional group. The remaining groups are given as low a number as possible by going around the ring. It is not necessary to indicate the position of the principal functional group while

2-Bromo-4-nitro
benzoic acid2,3-Dibromo
aniline2,6-Dibromo-4-chloro
aniline

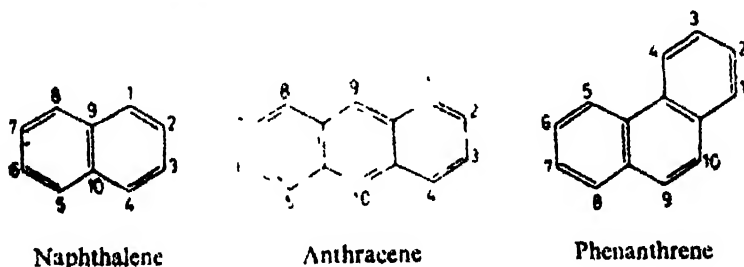
writing the name. In the event no trivial name is acceptable for a particular substituent, one is constructed by choosing the appropriate unbranched chain in the substituent. The numbering commences from the point of attachment of the substituent to the ring. The name is then ended with *-yl* and is used as *prefix* to the name of benzene.

1-Bromo-2-methylpropyl
benzene2-(3-Methylbutyl) benzene
(2-Phenyl-3-methyl butane)

The $\text{—C}_6\text{H}_5$ group, often has to be used as a substituent, i.e. as a *phenyl* group and the IUPAC rules for naming straight chain compounds are employed, as illustrated below:



Higher aromatic systems, known as *polycyclic aromatic hydrocarbons* behave similar to benzene and its derivatives. The carbon atoms in these molecules are numbered in a regular manner.



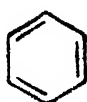
Note that there are four equivalent 1-positions in naphthalene and anthracene but there are only two in phenanthrene.

Occasionally, symmetrical compounds are named as biaryls or bialkyls. Such names indicate that the compounds contain two identical units joined together.



12.2 HÜCKEL RULE (AROMATICITY)

As stated earlier benzene and related compounds are aromatic. They possess high resonance energies and are very stable. This extra stability is conferred upon them due to a unique property called *aromaticity*. To predict whether a compound is aromatic or not, Hückel proposed a rule on the basis of molecular orbital calculations. According to the rule, familiarly known as the *Hückel rule*, a planar, conjugated, cyclic system containing $(4n+2)$ π electrons should be aromatic, where n is an interger. Since the inception of this rule, the aromaticity of a number of molecules has been predicted. Benzene and its derivatives, according to this rule possess $(4n+2)\pi$ or six electrons, are thus aromatic.



Benzene
 $n=1, 6\pi$ ele

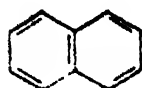


Toluene
 $n=1, 6\pi$ ele

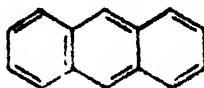


Phenol
 $n=1, 6\pi$ ele

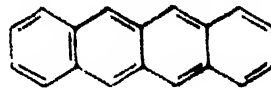
or an aromatic sextet. Polynuclear hydrocarbons i.e. containing more than one benzene ring and their derivatives are similarly aromatic



Naphthalene
 $n=2, 10\pi$ ele

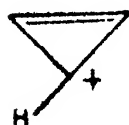


Anthracene
 $n=3, 14\pi$ ele

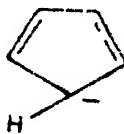


Naphthacene
 $n=4, 18\pi$ ele

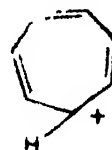
Further verification of the rule comes from the aromatic behavior of certain cyclic ions. The following ions exist as completely conjugated planar systems and obey Hückel rule



Cyclopropenyl cation
 $n=0, 2\pi$ ele



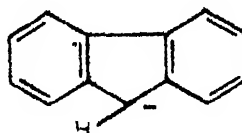
Cyclopentadienyl anion
 $n=1, 6\pi$ ele



Tropylium ion
 $n=1, 6\pi$ ele



Cyclooctatrienyl dianion
 $n=2, 10\pi$ ele



Fluorenyl anion
 $n=3, 14\pi$ ele

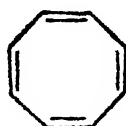
The cyclopropenyl cation with 2π electrons is aromatic and triphenylcyclopropenyl bromide has been isolated in the solid form. Cyclopentadiene and fluorene are highly acidic hydrocarbons. The tropylium ion (cycloheptatrienyl cation) has 6π electrons and exhibits aromatic character.

The heterocyclic compounds such as pyrrole, furan, thiophene, pyridine and quinoline, etc. similarly follow Hückel rule and are aromatic.

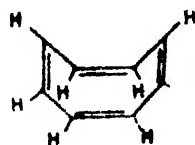
Cyclobutadiene a square planar molecule and cyclooctatetraene which possess an alternating system of single and double bonds would also be



Cyclobutadiene
 4π ele

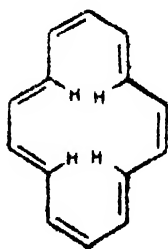


Cyclooctatetraene
 8π ele

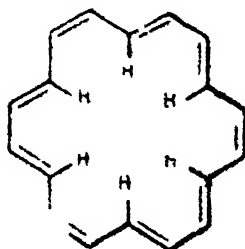


expected to be aromatic and stable. On the contrary cyclobutadiene contains only 4π electrons and is a highly reactive and non-aromatic compound. Cyclooctatetraene with 8π electrons does not also obey Hückel rule. It is, however, relatively stable compared to cyclobutadiene but possesses a low resonance energy (3.3 kcal/mole). There is no probability of electron delocalization and it behaves as a typical olefinic compound. This is so because spectroscopic analysis has shown that a planar cyclooctatetraene would have bond angles of 135° resulting in a considerable ring strain. It rather exists in a non-planar tub-shaped structure.

Monocyclic compounds having alternating system of single and double bonds have generally been referred to as *annulenes*. The ring size of an annulene is indicated by a number written in parenthesis. Thus cyclobutadiene, benzene and cyclooctatetraene are called as [4] annulene, [6] annulene and [8] annulene respectively. Large monocyclic rings such as cyclotetraheptaene or [14] annulene has been prepared but shows no aromatic behavior. The reason may be that the four internal hydrogen atoms prevent the ring from assuming a planar structure. Such ring systems are



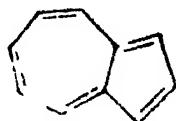
[14] annulene
 $n=3, 14\pi$ ele



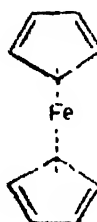
[18] annulene
 $n=4, 18\pi$ ele

referred to as *pseudoaromatic*. Cyclooctadecanonaene or [18] annulene, on the other hand is aromatic and possesses a high resonance energy. This confirms the generality of the Hückel rule.

Non-benzenoid Aromatic Compounds. The term aromatic includes all those compounds containing benzene rings. There are, however, compounds which possess an aromatic character (obey Hückel rule) but do not contain a benzene ring. Such compounds are designated as *non-benzenoid aromatics*. Cyclopentadiene, azulene, ferrocenes are some examples of this class.



Azulene
 $n=2, 10\pi$ ele



Ferrocene

12.3 PHYSICAL PROPERTIES OF AROMATIC COMPOUNDS

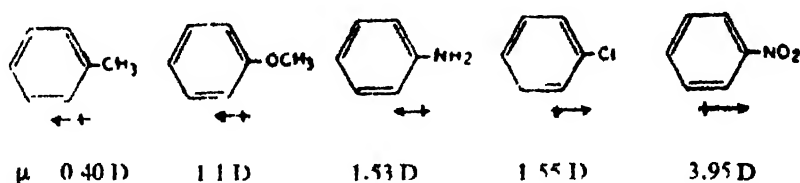
Many aromatic hydrocarbons possess a pleasant *aroma*. The lower members are liquid while higher members are crystalline solids (Table 12.1)

Table 12.1 Physical Constants of Aromatic Hydrocarbons

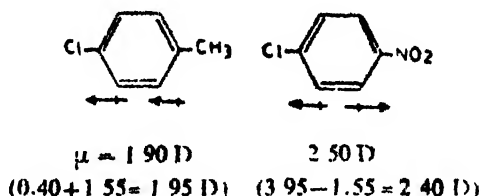
Hydrocarbons	m p , ($^{\circ}\text{C}$)	b p , ($^{\circ}\text{C}$)
Benzene		80
Toluene		110
Ethylbenzene		136
n-Propylbenzene		159
iso-Propylbenzene		152
t-Butylbenzene		169
o-Xylene		116
m-Xylene		139
p-Xylene		145
Styrene		145
Biphenyl	70	
Naphthalene	80	
Anthracene	217	
Phenanthrene	101	

The boiling points rise gradually with an increase in the number of carbon atoms. These are compounds of low polarity, insoluble in water but soluble in ether, benzene or carbon tetrachloride. They burn with a sooty flame which is characteristic of all aromatic compounds but not of most aliphatic compounds, and is due to the high carbon content of the former. They are used as solvents for fats, resins, iodine, etc. and in the manufacture of dyes, drugs and as industrial solvents.

The mono substituted benzenes possess appreciable values of dipole moments as is evident from the following compounds :



The direction as well as the magnitude of the net dipole moment of *p*-benzene derivatives can be deduced from the simple additive principle :

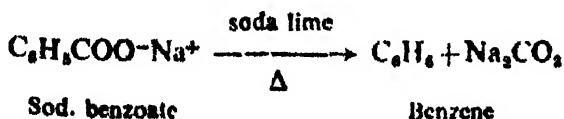


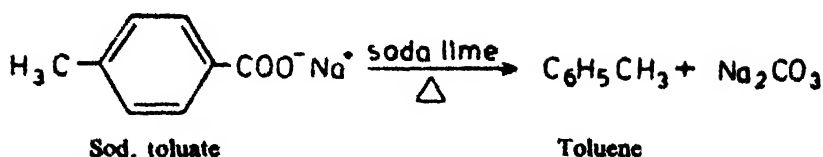
In the case of *p*-chlorotoluene both the component dipoles are operating in the same direction therefore, the net dipole moment is the sum of the individual dipole moments of chlorobenzene and toluene. For *p*-chloronitrobenzene the component dipoles operate in opposite directions and the net dipole moment is the difference of the two individual dipoles.

12.4 PREPARATION OF BENZENE AND ITS HOMOLOGUES

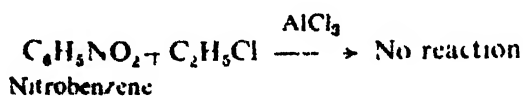
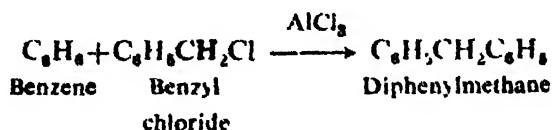
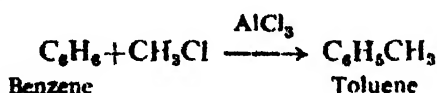
As a matter of fact there is no need to prepare benzene in the laboratory. Benzene is obtained from petroleum oil by cracking. Following methods, however, may be used for preparing benzene and its homologues.

1. By strongly heating the sodium salt of an aromatic carboxylic acid in the presence of soda lime ($\text{NaOH} + \text{CaO}$) decarboxylation, i.e., removal of CO_2 takes place with the formation of hydrocarbon.



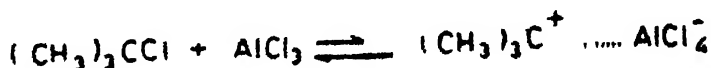


2. **The Friedel-Crafts Alkylation:** It is an important reaction for preparing aromatic hydrocarbons as it allows an alkyl group to be attached directly to the benzene ring. It employs benzene and an organic halide; AlCl_3 is a catalyst.

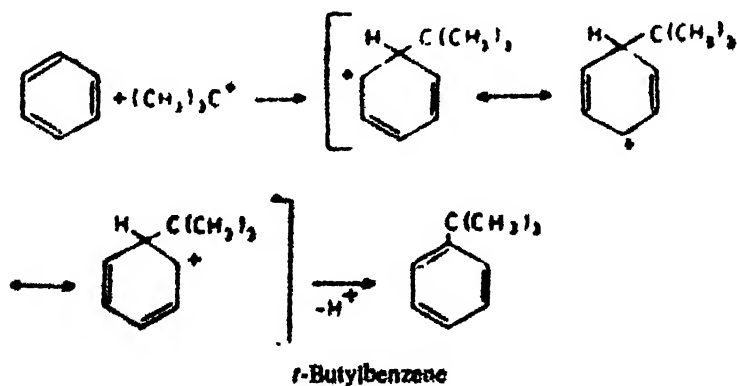


Mechanism

It is an electrophilic aromatic substitution reaction and the alkyl halide reacts with aluminum chloride to form a carbocation which subsequently attacks the aromatic ring. Aromatization of the resulting intermediate takes place by the loss of a proton.

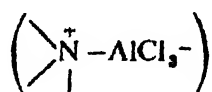


t-Butyl chloride



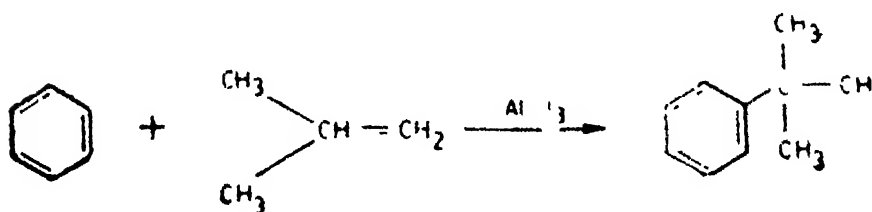
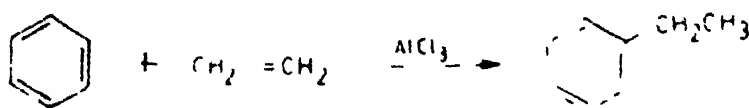
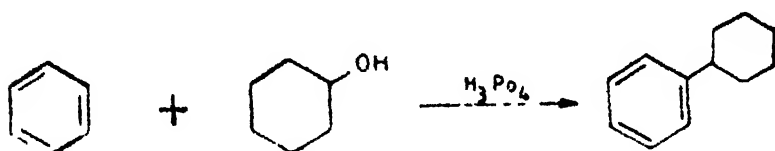
Depending on the structure of the alkyl halide the intermediate could be a discrete carbocation or a complex

Since a positive species attacks an aromatic ring, presence of electron-withdrawing groups such as $-\text{NO}_2$, CN on the aromatic ring retard the rate of the reaction. These groups greatly reduce the electron density on the ring. Nitrobenzene does not react in the Friedel-Crafts reaction. Certain electron-donating groups such as NH_2 , OH also deactivate the ring towards electrophilic attack. These groups complex with AlCl_3

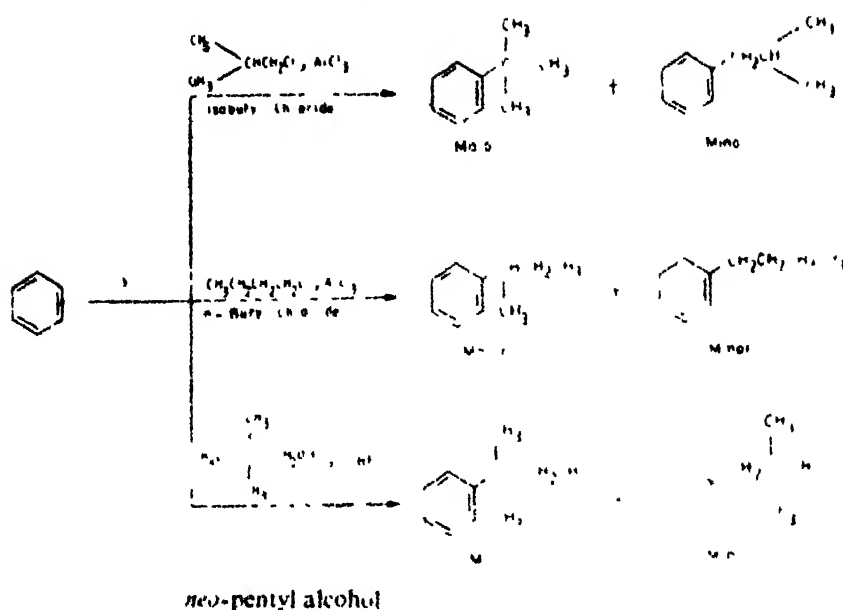


and thus diminish the electron-density of the ring.

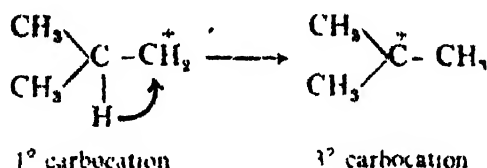
The choice of an alkylating agent is quite wide as protonated alcohols and alkenes also provide carbocations. This is exemplified by the accompanying reactions



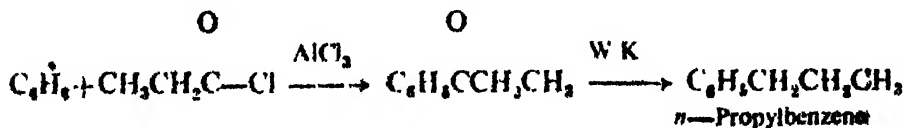
The Friedel-Crafts reaction is often accompanied by molecular rearrangements and a mixture of products is obtained. This is illustrated by the following examples.



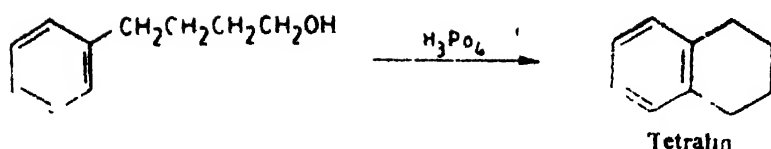
The rearranged product is formed in a major yield. This is possible because the initially formed carbocation undergoes a hydride (H^-) or an alkyl group shift to form a more stable carbocation.



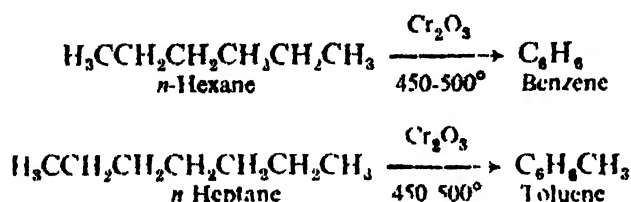
A pure sample of *n*-alkyl hydrocarbon is obtained by alternative methods. One such method requires the acylation of the ring followed by Wolff-Kishner reduction of the ketone.



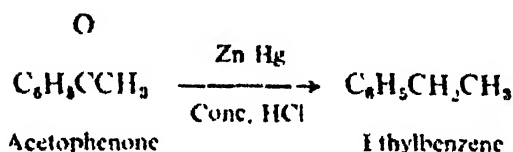
Intramolecular Friedel-Crafts reaction is also possible in which cyclic products are obtained. An example is the reaction of 4-phenyl-1-butanol to give tetralin.



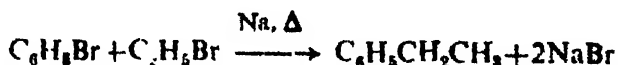
3. Dehydrogenation and cyclization of aliphatic hydrocarbons using Cr_2O_3 as a catalyst yields lower aromatic hydrocarbons. At the present time more toluene is produced commercially by this method than from coal tar.



4 *Clemmensen Reduction of Ketones.* Aromatic ketones can be reduced to hydrocarbons by the Clemmensen reduction (amalgamated zinc and conc. HCl). Acetophenone, for instance, yields ethylbenzene according to this reaction. Ketones can be readily obtained by the Friedel-Crafts acylation (Chapter 16).



5. *Wurtz-Fittig Reaction:* The alkylaryls can be obtained by heating an aromatic halide and an aliphatic halide in the presence of sodium in an inert solvent.



Several side-products are, however, obtained in this reaction.

6. *From Acetylene:* Benzene is obtained by passing acetylene through a red hot tube.



7. Lithium dimethylcuprate replaces iodine or bromine by methyl from aryl halides. This results in alkylation of the aromatic ring in high yields. Toluene can be obtained from iodobenzene in this manner.



8. *From Coal-tar:* For details see Section 12.11.

12.5 STRUCTURE OF BENZENE

The following evidence bears upon the structure of benzene.

1. Elemental analysis and molecular weight determination shows that the molecular formula of benzene is C_6H_6 .

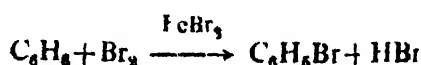
2. *Unsaturation in Benzene*

a. A saturated molecule should have a molecular formula C_nH_{2n+2} , according to C_nH_{2n+2} . The ratio of carbon to hydrogen in benzene indicates that the molecule is unsaturated. However, it neither responds to Baeyer's test nor does it decolorize bromine solution in carbon tetrachloride.

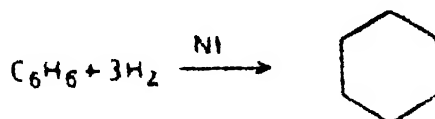
b. Benzene, when chlorinated in the presence of sun light, forms C_6H_5Cl . This indicates that three double bonds are present.

3. *Cyclic Structure of Benzene*

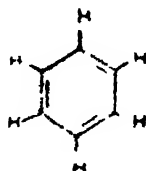
a. The above information shows that benzene is an unsaturated compound but it does not behave like alkynes or alkenes. Reaction between benzene and bromine and a trace amount of $FeBr_3$ yields a single compound, namely bromobenzene



b. Hydrogenation of benzene in the presence of Ni or Pd yields *cyclohexane*, by the uptake of 3 molecules of hydrogen.



These experiments suggest a cyclic structure for benzene. Faraday isolated benzene in 1825 but its presently accepted structure was first suggested by Kekule in 1865. He proposed that benzene is a regular hexagon in which an alternate system of single and double bonds is present.

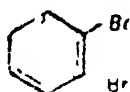


Kekule structure for benzene

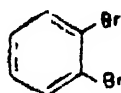
There are two objections against Kekule's structure:

a. Why is it that benzene shows such a remarkable stability toward oxidizing agents like $KMnO_4$ even though due to its double bonds it is expected to be reactive?

- b. The Kekule structure would predict only one mono bromobenzene but two 1,2—dibromobenzenes (I) and (II). In (I) there is a double bond

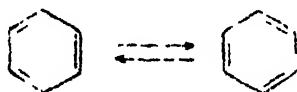


(I)



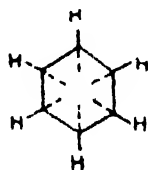
(II)

between the two bromine atoms while in (II) there is a single bond. Therefore, if Kekule's structure were correct, both of the isomers should exist and have different properties. But only one 1,2-dibromobenzene is known. To account for this, Kekule postulated a dynamic equilibrium between the two structures as shown below:

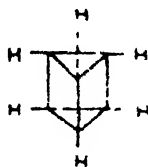


In other words, the position of single and double bonds are not fixed and instead they oscillate.

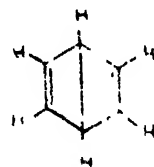
Several additional structures were also advanced during the nineteenth century but were soon rejected. One such structure (III) was due to Armstrong in which the valences were directed toward the center.



(III)



(IV)



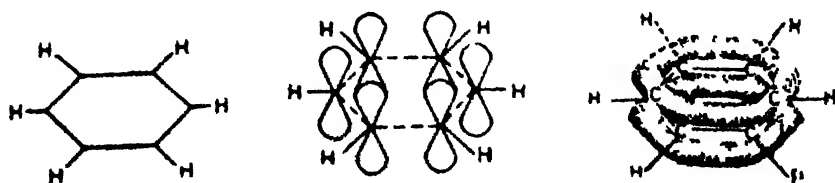
(V)

Another attempt was made by Ladenburg who suggested a prism structure (IV) in order to explain why benzene does not behave like an unsaturated compound. The third structure (V) was the diagonal formation of Dewar, but was rejected on the basis that it was not symmetrical. It is interesting to point out here that this structure was subsequently synthesized in 1963 by two American workers, van Tamelen and Pappas.

In summary, the Kekule structure withstood all the tests and has been further substantiated in the light of modern views about the structure of benzene.

Molecular Orbital Model for Benzene: Kekule suggested a dynamic equilibrium between the two structures of benzene as it is known but benzene now is a single molecule. This has been adequately interpreted by

the modern molecular orbital theory. Each carbon atom in benzene is sp^2 hybridized as in ethylene with a bond angle of 120° . There are six $2p_z$ atomic orbitals (one on each carbon atom) which are parallel to each other but are perpendicular to the plane of the ring and project above and below it. Each p_z orbital interacts equally with its two neighbours producing a



circular double-doughnut shaped M.O. embracing all six carbon atoms. The electrons are spread out since they tend to repel each other and we often say that the electrons in benzene are delocalized. Because six electrons are involved, therefore, six molecular orbitals are possible according to the LCAO treatment* as follows

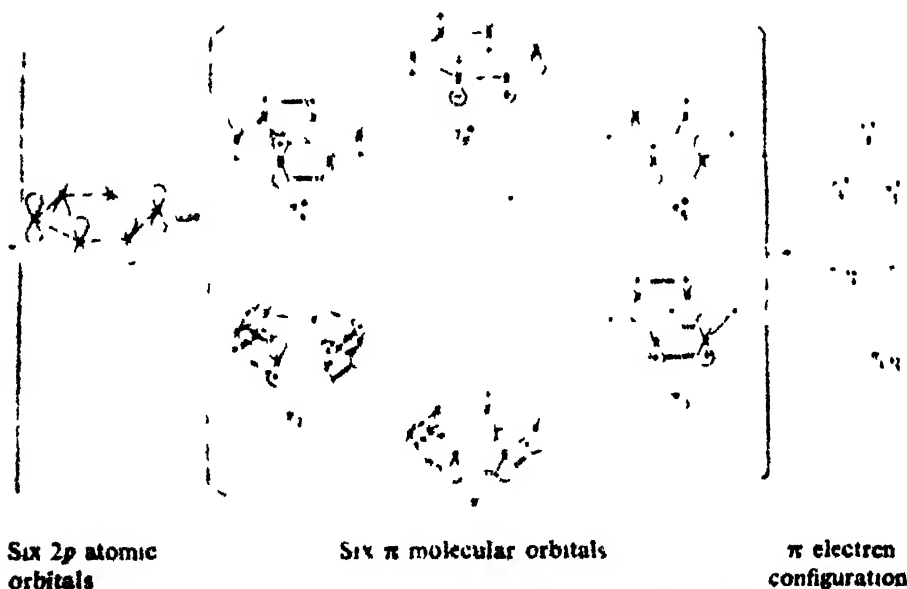


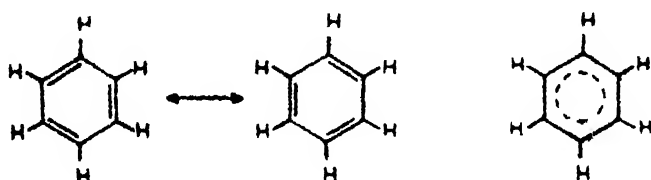
Fig. 12.1 Molecular orbital description of benzene

Three of the molecular orbitals are bonding and three are anti-bonding. Thus by placing the six valence electrons in the three bonding π -orbitals, with not more than two electrons in any one orbital, a model for benzene is

*In the LCAO (Linear combination of atomic orbitals) treatment of the overall molecular orbitals are approximated by simple addition and subtraction of individual molecular orbital. The terminology was suggested by R.S. Mulliken.

constructed which has all the structural features of Kekule's proposed structure and in addition can be treated by molecular orbital calculations and is thermodynamically very stable.

Resonance in Benzene: There is another term used for delocalization and is called resonance. As stated earlier we say that a condition of resonance exists in benzene and that it is stabilized by resonance. The theory of resonance was developed a few years prior to the molecular orbital treatment. Thus resonance has provided a useful method of describing molecules like benzene. Benzene is represented as a resonance hybrid of the following two equivalent structures



Resonance hybrid of benzene

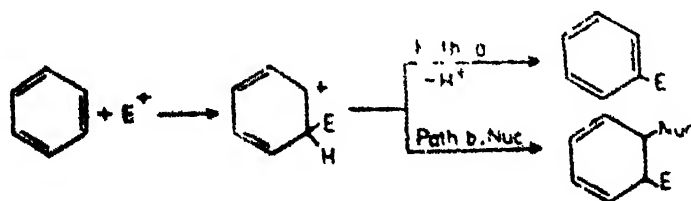
One observes that they involve identical positions of the atoms and differ only in their electronic arrangement. It is believed that the structure of benzene is *hybrid* of the two structures and is not identical with either of the two structures. The C--C bond is neither single nor double, but is considered a 'partial double bond'. Resonance stabilizes the molecule against a number of chemical reactions.

The six hydrogen atoms are chemically equivalent. The C--H bond distance is 1.084\AA and the carbon-carbon bond distance is 1.39\AA which is intermediate between the carbon-carbon bond distance of a saturated hydrocarbon (1.54\AA) and an alkene (1.34\AA).

12.6 REACTIONS OF BENZENE AND HOMOLOGUES

Benzene and its homologues undergo a series of interesting reactions.

1. **Substitution Reactions.** The most important reaction of benzene is electrophilic substitution on the benzene ring. Several types of reagents yield substitution products. All follow similar reaction pathways. An electrophile (E^+) attacks the benzene ring to form an intermediate carbonium ion which has two paths available to it. In path (a) the ion can stabilize itself by losing a proton and yield a substitution product. In path (b) it can react with a nucleophile and thus afford an addition product. Generally path (a)



is favored over path (b) so that one usually observes only substitution reaction. In this path the aromaticity of benzene ring is preserved. This is shown in the potential energy diagram in which the dotted line refers to the higher energy product involving a higher transition state.

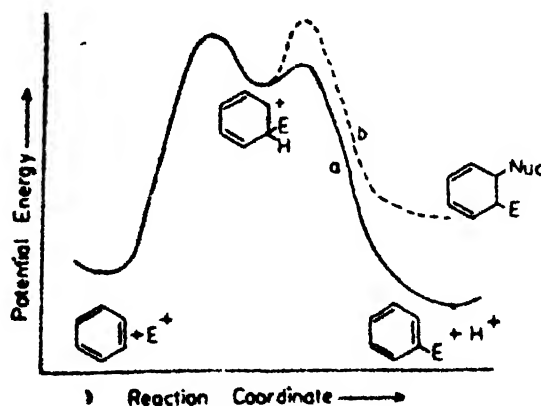
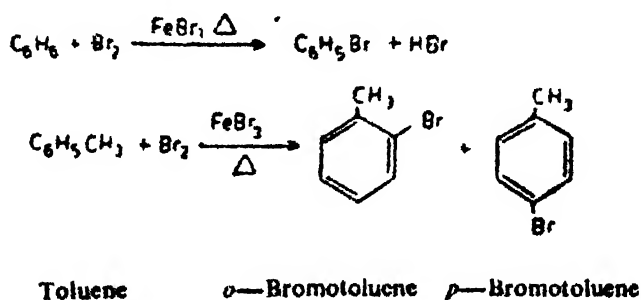


Fig. 12.2 Potential energy diagram for a substitution reaction

a. **Halogenation:** Bromine or chlorine reacts with benzene in the presence of a Lewis acid to form bromo- or chloro-benzene.

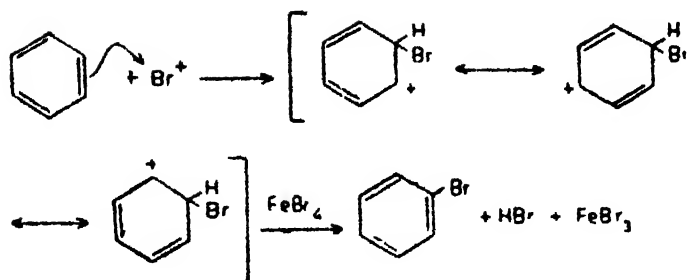


Lewis acid acts as a catalyst and helps to polarize the halogen molecule by accepting a lone pair from it and is called a 'halogen carrier'. The positive end of the halogen molecule is now an electrophile and attacks the benzene ring. The reaction does not proceed with iodine because the position of equilibrium is unfavorable and lies to the left.

Mechanism

The mechanism starts with the formation of a *bromonium ion*, Br^+ which attacks the benzene ring to form the *benzenebromonium ion* which is



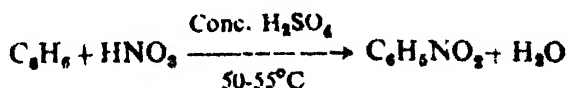


stabilized by resonance. In the final step a proton is lost with the help of FeBr_4^- to form bromobenzene and hydrogen bromide. At the same time this step regenerates the catalyst FeBr_3 . Iodination though occurs without a Lewis acid but the reverse reaction is much faster than iodine substitution in the ring, and no iodobenzene is obtained.

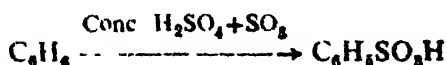


In case of toluene two products are obtained. The directive effects of sulfuric acid, groups will be taken up in Section 12.7.

b. *Nitration*: A nitro group can be introduced into a benzene ring using a mixture of conc. nitric and sulfuric acid (1 : 2 ratio). In the absence of H_2SO_4 the reaction is slow.

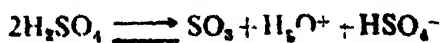


c. *Sulfonation*: Benzene reacts at room temperature with fuming sulfuric acid, i.e. conc., sulfuric acid containing dissolved SO_3 , forming benzene sulfonic acid. This reaction requires no catalyst.

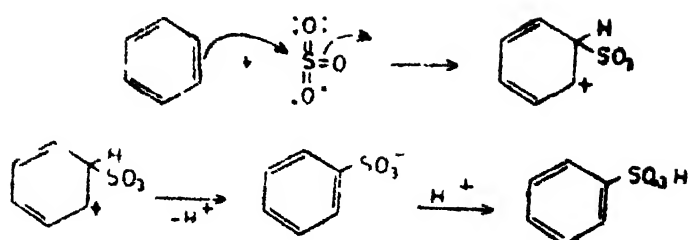


Mechanism

In conc. H_2SO_4 , sulfur trioxide is produced as follows:

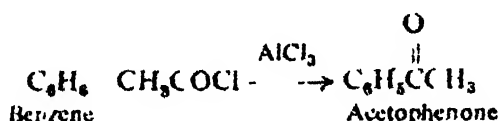


Fuming sulfuric acid is the most common sulfonating agent. Because the three $\text{S}=\text{O}$ bonds in SO_3 are all polarized (S^+-O^-) and the cumulative charge on the sulfur atom is highly positive. Therefore sulfur trioxide which is the attacking species is a powerful electrophile. The importance of sulfonation reaction lies in the fact that the $-\text{SO}_3\text{H}$ group can be replaced by $-\text{OH}$ to form phenols. Sulfonation is also important in the manufacture of detergents.



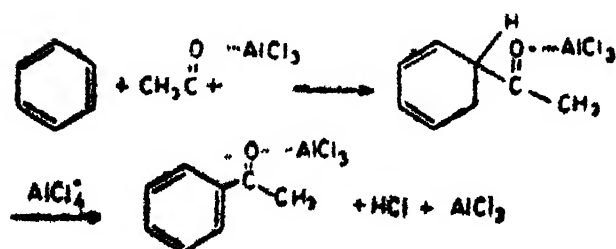
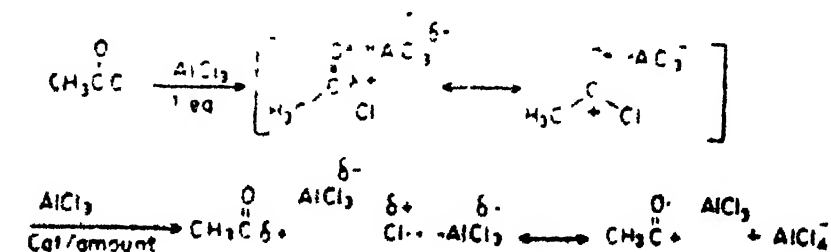
d. *Friedel-Crafts Acylation*: Introduction of an acyl group on the benzene ring under the Friedel-Crafts conditions was discussed on p. 192

An acyl group ($-\text{C}-\text{R}$) can similarly be introduced using an acyl halide and anhydrous aluminum chloride. The process is called *acylation*

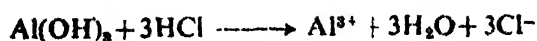
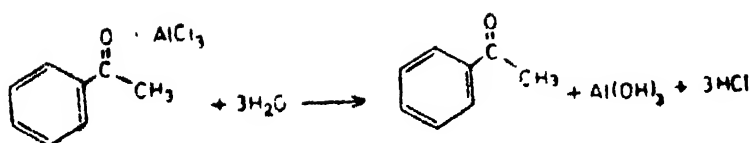


Mechanism

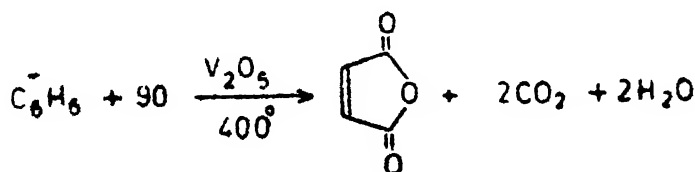
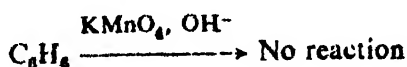
Anhydrous AlCl_3 , being a Lewis acid, coordinates with the unshared pair of electrons of the carbonyl oxygen. Further reaction with catalytic amounts



of AlCl_3 forms the electrophile which attacks the benzene ring. The carbonyl group is still complexed with AlCl_3 and ketone is liberated on hydrolysis with cold dil. hydrochloric acid.



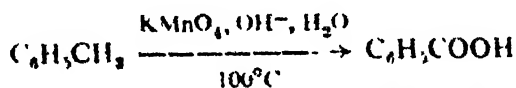
2. *Oxidation*: Benzene itself is resistant to oxidation, a KMnO_4 solution to which benzene has been added remains purple colored. However, on oxidation with air in the presence of V_2O_5 , maleic anhydride is formed



Benzene

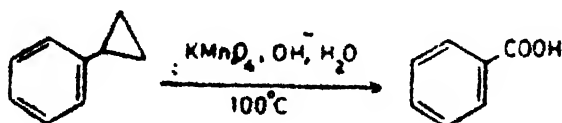
Maleic anhydride

The benzene homologues, however, are oxidized to the corresponding carboxylic acids.



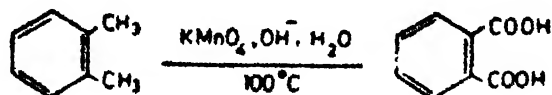
Toluene

Benzoic acid



Cyclopropylbenzene

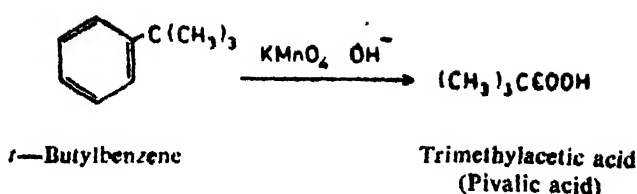
Benzoic acid



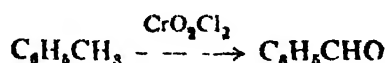
m-Xylene

Phthalic acid

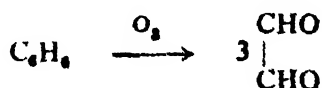
If there is no benzylic hydrogen available, then the side-chain resists vigorous oxidation. For instance, oxidation, under vigorous conditions of *t*-butylbenzene results in trimethylacetic acid—the product of oxidation of the benzene ring.



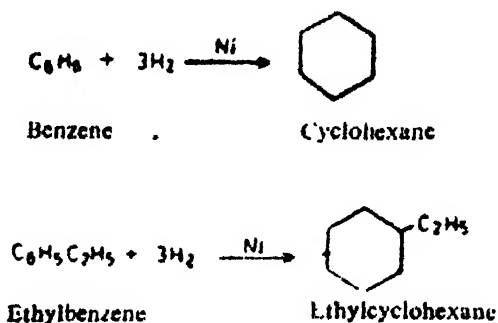
A milder oxidizing agent such as chromyl chloride converts $-\text{CH}_3$ group of toluene to an aldehyde.



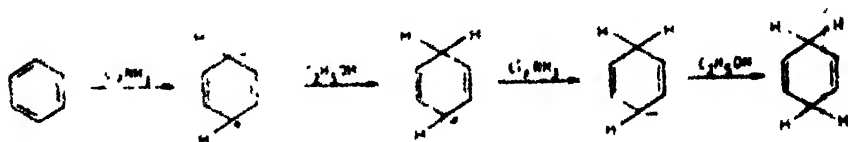
Ozonolysis of benzene yields 3 molecules of glyoxal



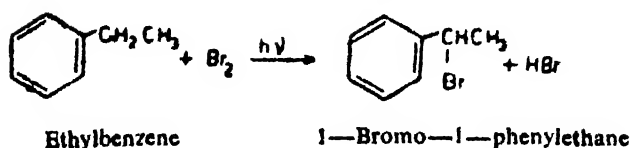
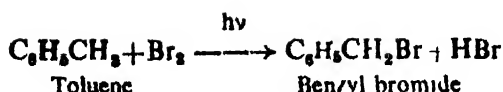
3. Catalytic Hydrogenation: Benzene and its homologues are reduced by hydrogen in the presence of Ni catalyst.



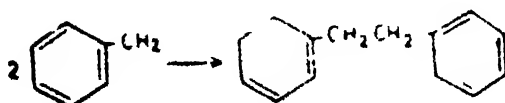
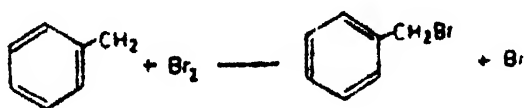
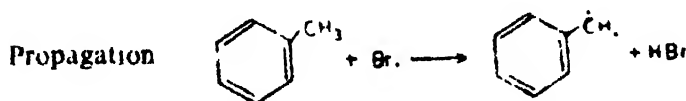
Benzene ring can also be reduced partially. This is accomplished by using a metal-ammonia-alcohol mixture as reducing agent. This reagent is powerful enough to reduce benzene and also specific to add only two hydrogen atoms. Benzene is reduced with lithium and liq. ammonia in ethanol to cyclohexa-1,4-diene. This is called the *Birch reduction*. The reaction is considered to proceed *via* an anion radical mechanism.



4. Radical Halogenation: Benzene homologues undergo halogenation under the catalytic effect of u.v. light or a radical initiator. The products obtained are different than those in the case of ionic halogenation.

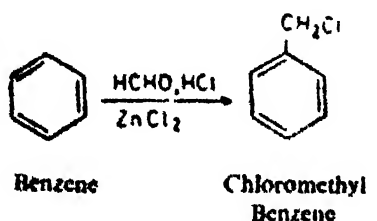
**Mechanism**

The mechanism of free radical halogenation of toluene can be formulated as follows:

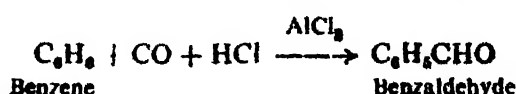


The bromine atom formed by the cleavage of the Br—Br bond abstracts a hydrogen atom from the methyl group of toluene to form benzyl radical. This in turn reacts with bromine to form the product. The formation of the product in the reaction is governed by the stability of the intermediate radical which follows the order $3^\circ > 2^\circ > 1^\circ$.

5. **Chloromethylation:** Certain other reactions of aromatic nucleus are related to the Friedel-Craft reaction. The introduction of a chloromethyl group is brought by HCHO, HCl and 2. Cl_2 .

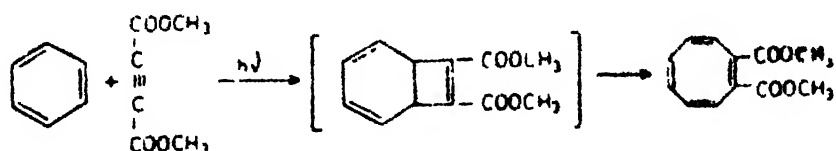


6. *The Gatterman-Koch Reaction*: Benzaldehyde is obtained by the treatment of benzene with CO and HCl in the presence of AlCl_3 . This

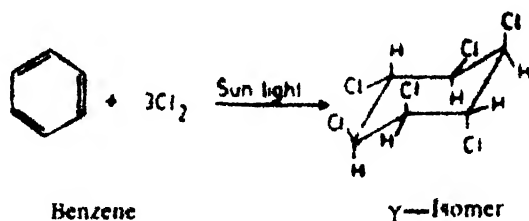


reaction probably involves a species of the type $\text{HC}^+ \rightleftharpoons \text{O} \cdots \cdots \text{AlCl}_4^-$.

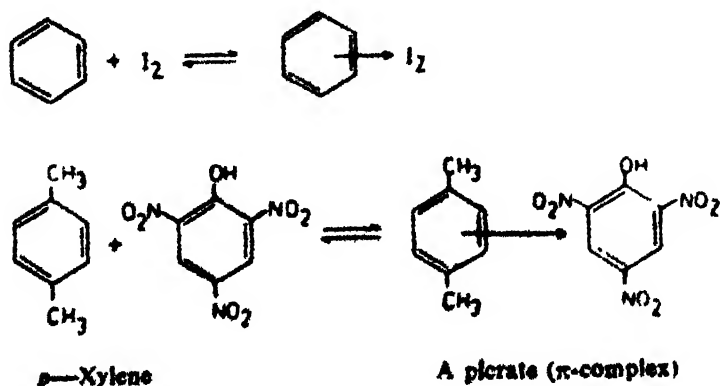
7. *Photo Addition*: Benzene undergoes exclusive addition in certain photochemical reactions and on irradiation with u.v. light, adds on dimethyl-acetylene-dicarboxylate, which being unstable decomposes to give a cyclo-



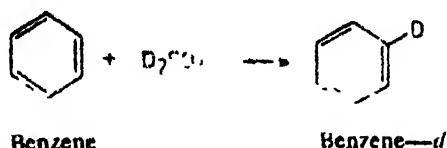
octatetraene derivative. Photochemical chlorination of benzene gives addition rather than substitutions product, gammaxane which is used as an insecticide against many agricultural pests. The activity is due to the presence of the γ -isomer, one of the geometrical isomers of $\text{C}_6\text{H}_6\text{Cl}_6$.



8. Benzene and other aromatic compounds form π -complexes with reagents such as iodine, picric acid, tetracyanoethylene, etc



9. Monodeuterobenzene is obtained by the reaction of benzene with deuteriosulfuric acid (D_2SO_4). The reaction as compared to sulfonation occurs under milder conditions.



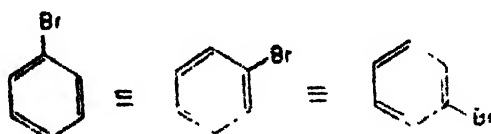
This reaction is also an example of electrophilic substitution process

12.7 USES OF BENZENE AND HOMOLOGUES

Benzene and toluene are used as solvents for fats, resins and in the laboratory are used in the preparation of insecticides and explosives (TNT).

12.8 DIRECTIVE EFFECTS OF SUBSTITUENTS AND REACTIVITY

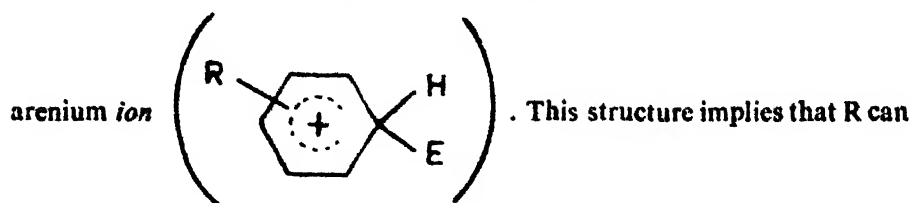
It was stated previously that in benzene all the six hydrogen atoms are chemically equivalent and a single product is obtained during an electrophilic attack on the nucleus, i.e. a single bromobenzene is obtained on bromination. Thus the following structures are all equal. But if a group is



already occupying a position on the ring, i.e., it is a benzene derivative, the incoming electrophile may attack either *ortho*, *meta* or *para* position relative to the attached group to yield a mixture of products. Since an electrophile is an electron-deficient species, it has a tendency to attack a position of high electron density. A substituent present on the benzene ring thus can cause the benzene derivative to react faster or slower than benzene itself by increasing or decreasing the electronic charge and the substituent is said to have an *activating* or *deactivating* effect. An electron donating group is activating while an electron-withdrawing group is deactivating. The former type of derivatives would react faster than the latter type in an electrophilic substitution reaction. A logical way to delineate the directing effect of a substituent has been developed qualitatively based on conjugation and polar effects of the substituent present on the ring.

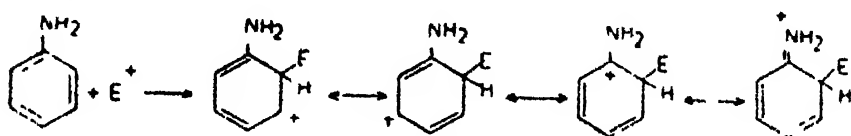
The various groups (see Table 12.2) have been divided into two types, i.e., electron-donating and electron-withdrawing. Those that withdraw electrons inductively are said to exert an $-I$ effect and those which withdraw electrons conjugatively a $-M$ effect. The terms $+I$ and $+M$ are assigned to electron-donating groups. The rationale in determining the directive

effects lies in writing different resonance structures of the intermediate

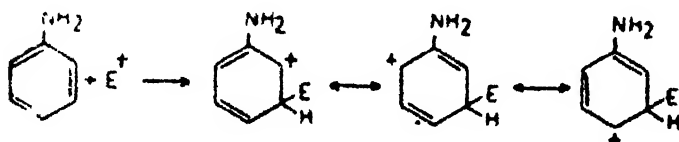


be in any position relative to the electrophile E. Then a decision is made on the basis of the most stable arenium ion formed. This is illustrated for attack of an electrophile (E^+) on aniline in which —NH_2 is an electron-donating group. Let us assume that the electrophile attacks all the three

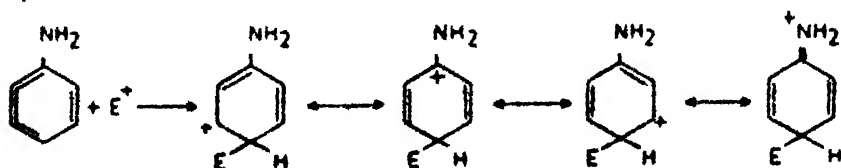
ortho



meta



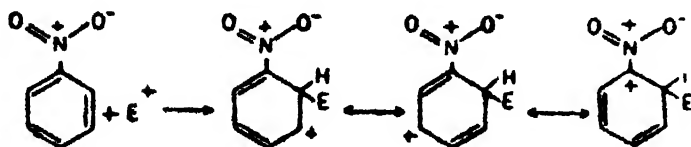
para



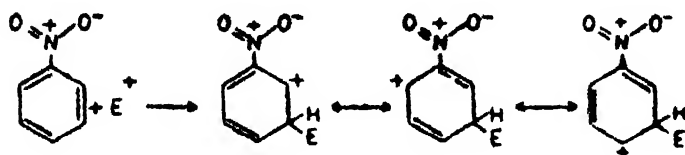
different positions on the benzene ring. A careful look at these intermediates indicates that the structures in which attack takes place at the *ortho* and *para* positions are more stable than those in which the attack is at the *meta* position because of the additional resonance structures of the positive charge with the amino group in the former case. Though the amino group is electron-withdrawing inductively ($-I$) but the resonance effect ($+M$) is far more important and that makes the amino group an effective electron-donating group. The amino group thus directs an incoming electrophile at the *ortho* and the *para* positions. It may thus be concluded that an electron-donating group is *ortho* and *para* directing. The nitro group is a powerful electron-withdrawing group and it does so both by inductive and resonance

effects. In order to see how this group directs the incoming electrophile we need to examine the resonance structures for the following arenium ions.

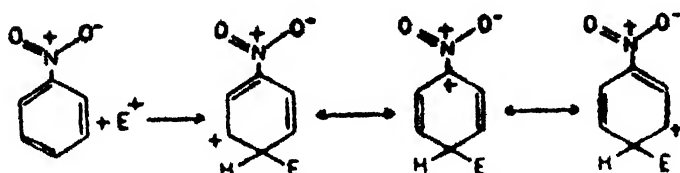
ortho



meta



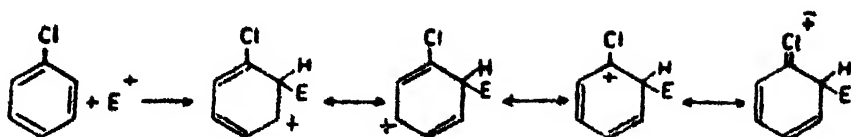
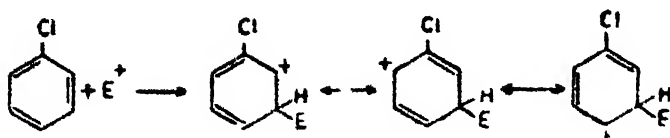
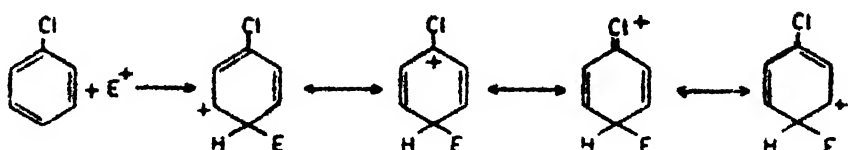
para



From these structures it is apparent that attack of an electrophile at the *ortho* and *para* positions requires the positive charge to be placed on the carbon atom bearing the electron-withdrawing group; such structures would thus be of high energy and unstable. The *meta*-substituted arenium ion is more stable because no such unstable structures contribute to its hybrid. The *meta*-substitution is thus favored in the case of the nitro group.

There are certain groups whose polar effects alter depending on the demand of the reaction. These substituents include halogens, nitroso and phenyl groups. Halogens are electron-withdrawing (I) that is why substitution of chlorine for hydrogen in acetic acid arguments the acidity of chloroacetic acid. But in electrophilic aromatic substitution halogens are *ortho* and *para* directing because the halogen atom, due to resonance interaction with the positive charge, stabilizes the arenium ion.

It does so in the same manner as the $-OH$ and $-NH_2$ groups by donating an unshared pair of electrons. These electrons result in relatively stable resonance structures contributing to the hybrids for the *ortho* and *para* arenium ions as shown below:

ortho*meta**para*

Although, according to resonance effects it may be anticipated that halobenzenes are more reactive than benzene, it is rather the reverse that is observed.

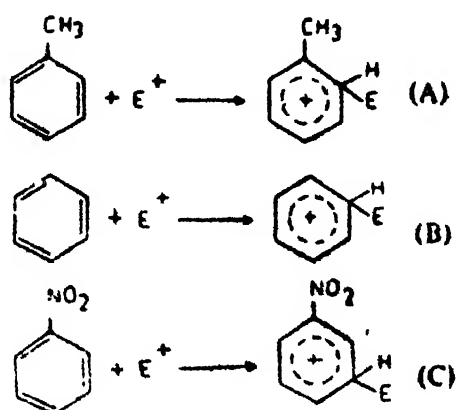
Thus the resonance effects determine orientation in halobenzenes whereas the inductive effect influences reactivity. Certain groups are *meta* directing by virtue of their electron-withdrawing nature, these include $-\text{CF}_3$, $-\text{N}^+(\text{CH}_3)_3$, $-\text{CCl}_3$ etc. The alkyl groups are electron-donating and direct the incoming electrophile to the *ortho* and *para* positions. The alkyl groups enter into hyperconjugation with the ring and thus act as electron-donors. The information discussed above is summarized in Table 12.3.

Table 12.3

Substituent	Polar Effects	Directing Effects
$-\text{NH}_2$, $-\text{OH}$, $-\text{OCH}_3$, $-\text{NHCOCH}_3$ $-\text{OCOCH}_3$	$-\text{I} + \text{M}$	<i>o</i> and <i>p</i>
$-\text{NO}_2$, $-\text{COOH}$, $-\text{COOR}$	$-\text{M}$	<i>m</i>
F, Cl, Br, I, $-\text{C}_6\text{H}_5$	$-\text{I} + \text{M}$	<i>o</i> and <i>p</i>
$-\text{CH}_3$, $-\text{C}_2\text{H}_5$, $-\text{CH}(\text{CH}_3)_2$ $-\text{C}(\text{CH}_3)_3$, cyclopropyl	$+\text{I} + \text{M}$	<i>o</i> and <i>p</i>
$-\text{CF}_3$, $-\text{CCl}_3$, $-\text{N}^+(\text{CH}_3)_3$	$-\text{I}$	<i>m</i>

This theory applies for mono substituted benzene derivatives, in case two similar groups are present they reinforce the activating or deactivating effects but if the groups are dissimilar then they compete with each other.

From the above discussion it is clear that certain groups are more activating than others. With respect to benzene, therefore, activating groups facilitate the attack of an electrophile on the ring while the deactivating groups render the attachment more difficult. Since the intermediate *arenium ion* formed is positively charged, electron-donating groups are capable of stabilizing it with the resultant decrease in activation energy of the transition state. To illustrate this point let us consider the attack of an electrophile (E^+) individually on toluene, benzene and nitrobenzene.



Out of these three intermediates, (A) will have the lowest and (C) the highest energy compared to (B). This information can be understood with the help of a potential energy diagram.

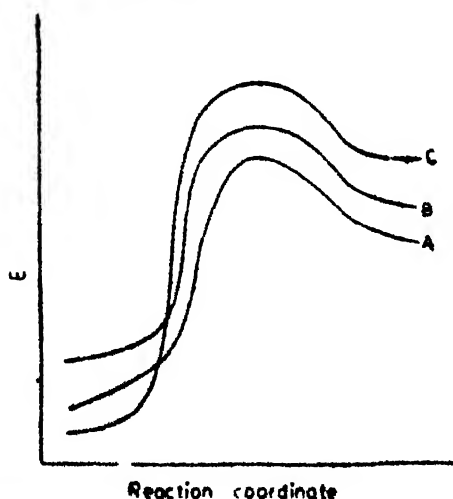


Fig. 12.3 Relative potential energies of the intermediates A, B and C.

The inductive and the resonance effects of the nitro group together make the energy of activation for an electrophilic attack on nitrobenzene much larger than that for benzene and toluene. This energy for toluene is even smaller than for benzene because of the activating effect of the methyl group.

12.9 NAPHTHALENE

Two benzene rings fused at the *ortho* positions form the naphthalene ($C_{10}H_8$) molecule. It has the same kind of bonds as benzene except that there are 10 electrons extending over a framework of ten carbon atoms. The isomeric mono substituted naphthalenes are distinguished by the numerals 1 and 2 or by the Greek letters α and β as shown below:

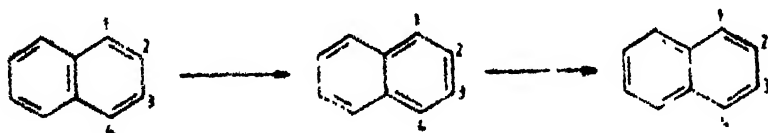


All the four α -positions are alike as are all the β -positions, thus there is only one α -derivative and one β -derivative of naphthalene. There are only two mono-derivatives, i.e. α and β possible for naphthalene whereas there are ten disubstituted and 14 trisubstituted derivatives. It complies with the Hückel rule, possesses aromatic stability and has resonance energy of the order of 60 kcal/mole.

12.9.1 Physical Properties

Naphthalene is a solid crystalline substance of melting point 80° and possesses a characteristic odor. It is insoluble in water but is soluble in boiling ethanol and benzene. It sublimes readily on heating.

Naphthalene is considered as a resonance hybrid of three canonical structures in which the C-C bonds are not identical. The bond distance

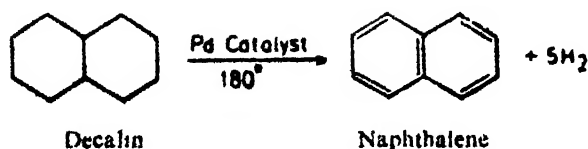


between C_1 - C_2 (1.365 \AA) is shorter than C_2 - C_3 (1.404 \AA) bond. An examination of the above resonance structures reveals that two structures have a double bond between C_1 - C_2 and only one between C_2 - C_3 . Therefore, the C_1 - C_2 bond distance is shorter, Naphthalene is also more reactive than benzene because of the difference in bond lengths.

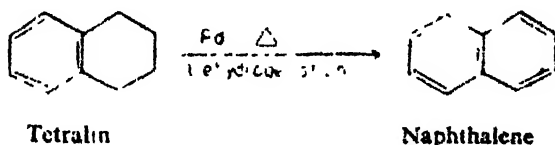
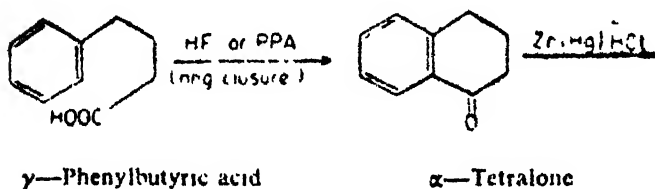
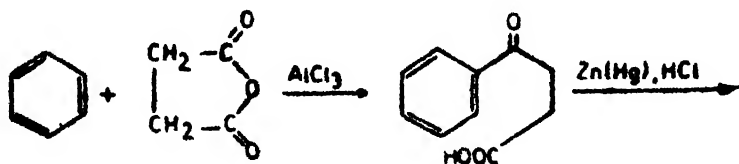
12.9.2 Preparation

1. Naphthalene is obtained predominantly from coal tar (for details see

Section 12.11.2). It may be prepared from decalin by dehydrogenation in the presence of a catalyst.



2. *Haworth Synthesis*: This involves a Friedel Crafts reaction between benzene and succinic anhydride and the resulting acid is reduced under

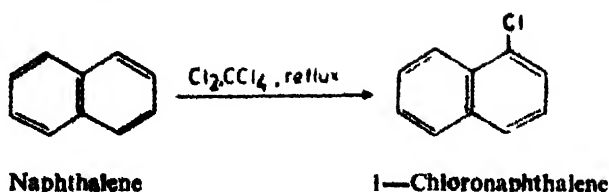


Clemmensen conditions and the ring is closed to α -tetralone with subsequent reduction and dehydrogenation yields naphthalene.

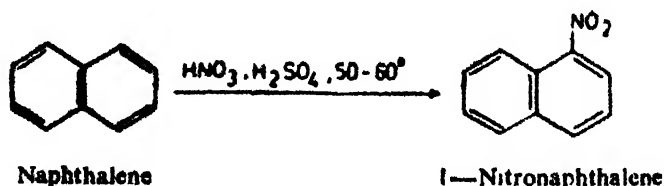
12.9.3 Reactions

1. *Electrophilic Aromatic Substitution*: Like benzene naphthalene undergoes halogenation, nitration, sulfonation and Friedel-Crafts reaction.

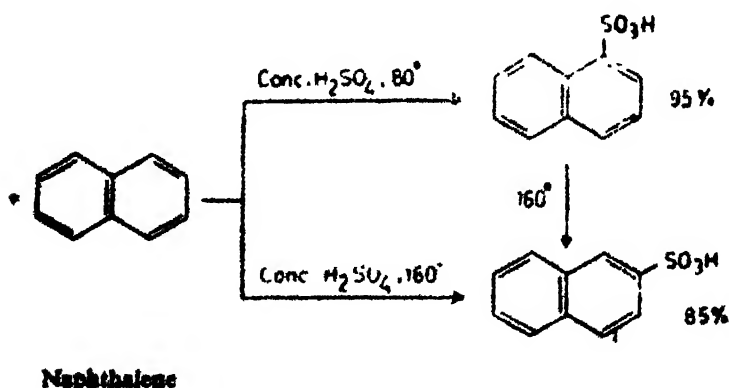
a. *Halogenation*: Chlorination or bromination occurs readily and no Lewis acid catalyst is required. The reaction takes place exclusively at the 1-position. The tendency of naphthalene to substitute at 1-position in preference to 2-position is usually explained on the basis of resonance stabilization of the intermediate carbonium ion as was done in the case of benzene. When the attack in naphthalene is at position-1, the intermediate ion is more stable.



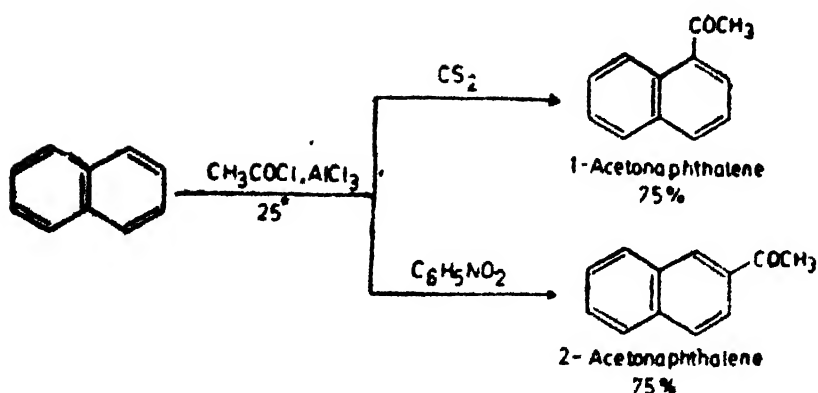
b. Nitration: Nitration ($\text{HNO}_3, \text{H}_2\text{SO}_4$) in naphthalene also occurs readily at 1-position:



c. Sulfonation: The orientation in sulfonation in naphthalene changes with the temperature of the reaction, at 80° mainly 1-naphthalenesulfonic acid is obtained while 2-naphthalenesulfonic acid results at 160° . Rapid formation of the 1-isomer in the sulfonation of naphthalene reflects the greater stability of the intermediate carbonium ion. When 1-naphthalene-sulfonic acid is heated at 160° most of it is converted to 2-naphthalene-sulfonic acid. The sulfonic acid group at position-1 is sterically hindered by the hydrogen in the 8-position. The unhindered 2-isomer is the more stable of the two naphthalene sulfonic acids.



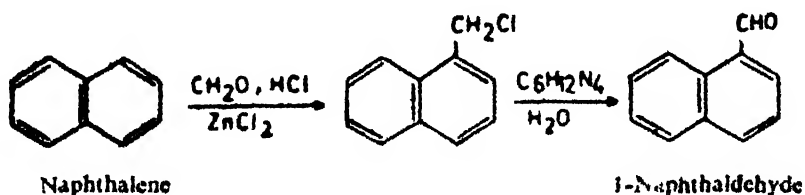
d. Friedel-Crafts Acylation: The orientation of F.C. acylation depends on the nature of the solvent. Thus naphthalene, on acylation ($\text{CH}_3\text{COCl}, \text{AlCl}_3$) in carbondisulfide yields the 1-isomer while predominantly 2-isomer is obtained in nitrobenzene as solvent. The difference in orientation is



Naphthalene

attributed to the formation of a bulky addition complex in nitrobenzene which tends to attack the more spacious 2-position, because there is steric interference at position—1 by the hydrogen at 8-position.

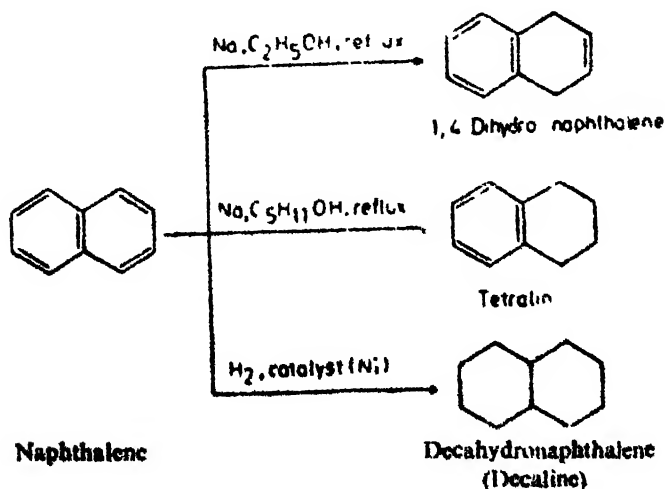
c. **Chloromethylation:** Chloromethylation, i.e., introduction of a CH_2Cl group takes place easily and subsequent treatment with hexamethylenetetramine ($\text{CH}_2\text{O} + \text{NH}_3$) yields an aldehyde.



Naphthalene

1-Naphthaldehyde

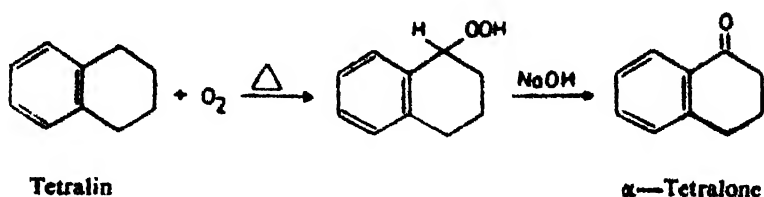
2. **Reduction:** Different reducing agents reduce naphthalene to varying degrees.



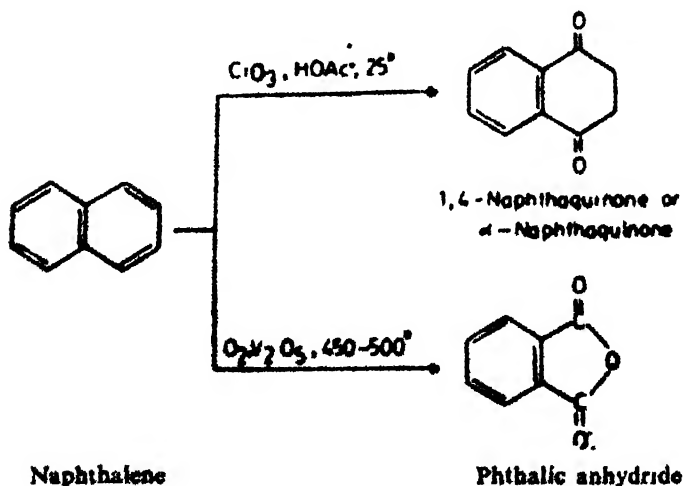
Naphthalene

Decahydronaphthalene
(Decaline)

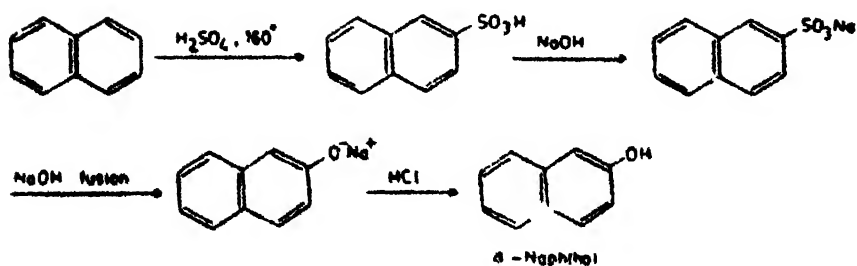
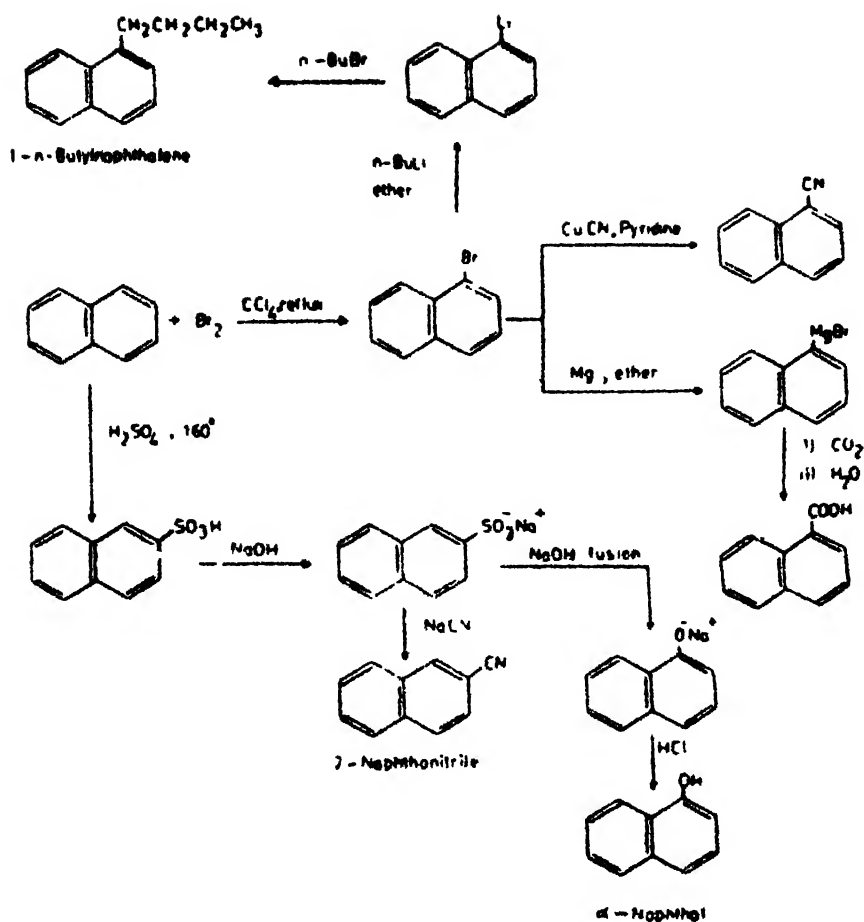
Heating tetralin in air for 50 hours at 70° and decomposing the peroxide so formed with sodium hydroxide yields α -tetralone.

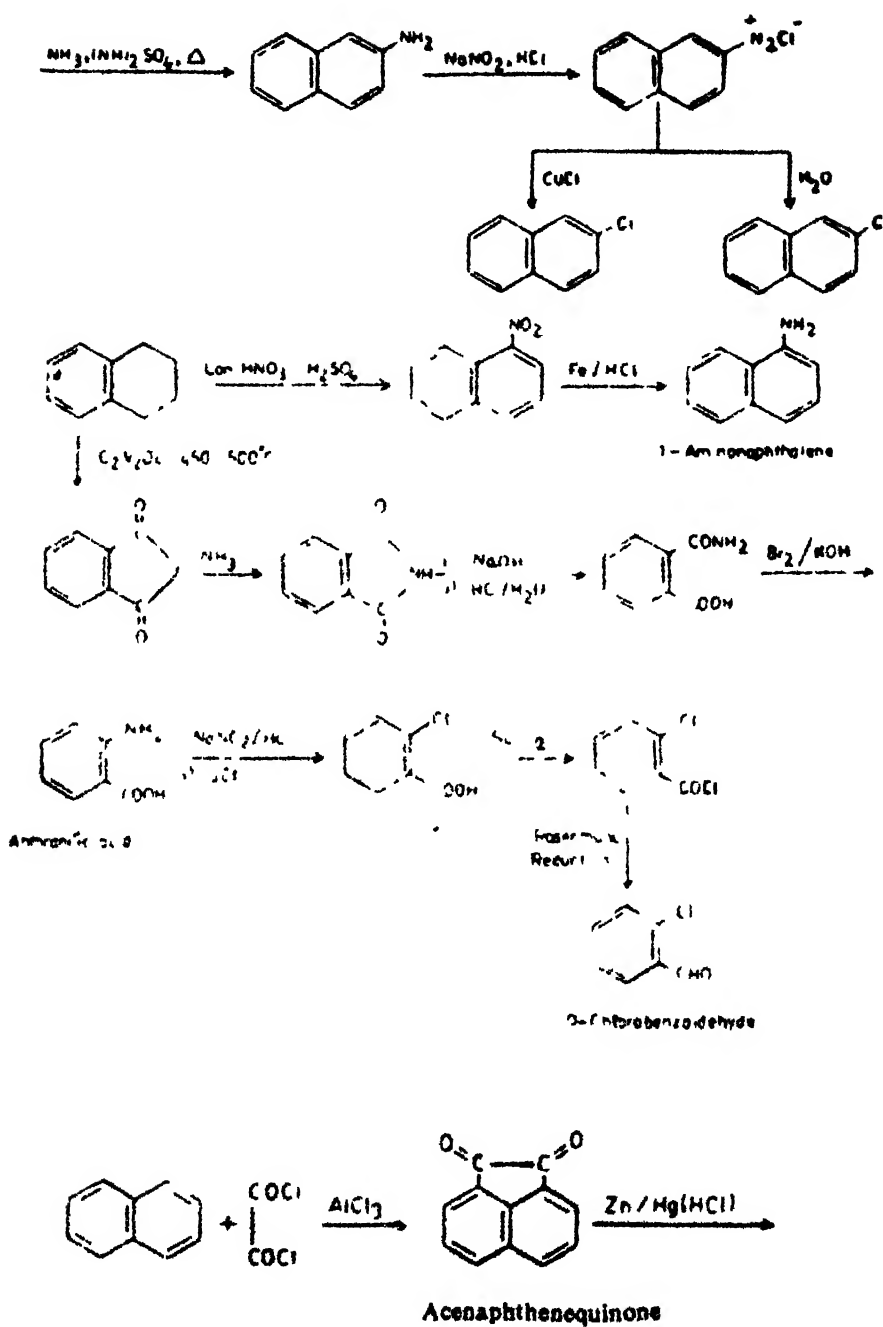


3. Oxidation: Oxidation of naphthalene by different oxidizing agents produces different products. Under milder conditions, 1,4-naphthaquinone is obtained while vigorous oxidation yields phthalic anhydride. In the latter oxidation, phthalic acid is initially formed which loses water immediately to give phthalic anhydride.



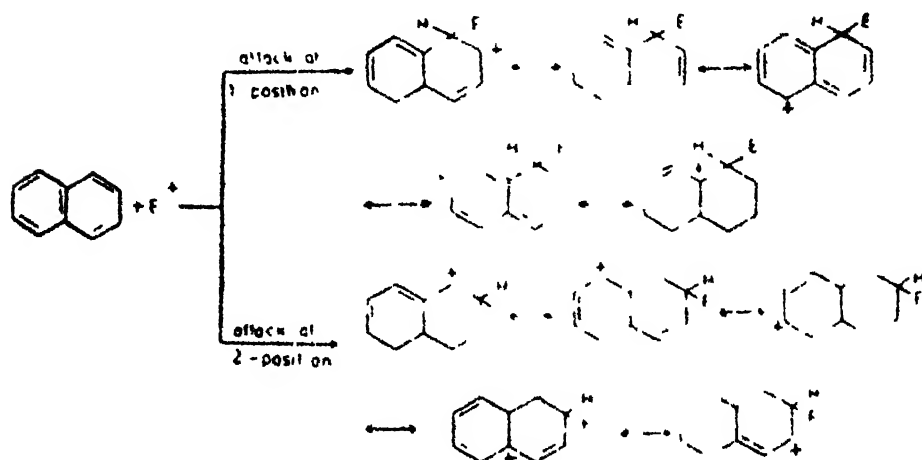
4. Naphthalene Derivative: The different α - and β -substituted derivatives of naphthalene can be prepared by the following sequence of reactions:





12.9.4 Orientation in Naphthalene

The distribution of isomers in an electrophilic substitution can be predicted on the basis of the stability of the intermediate ion formed. Let us consider the attack of an electrophile (E^+) at the 1- and 2-positions on naphthalene. The resonance structures for the σ -complex can be written as follows:



Naphthalene

An examination of these structures indicates that the benzene ring is preserved in two resonance structures for attack at 1-position but in only one for attack at the 2-position. The electrophilic attack thus takes place exclusively at 1-position in naphthalene.

12.9.5 Uses of Naphthalene

Naphthalene is used as an insecticide to prevent moths in clothes. It is also used for the manufacture of dyes. Tetralin and decalin are used as solvents for paints and varnishes.

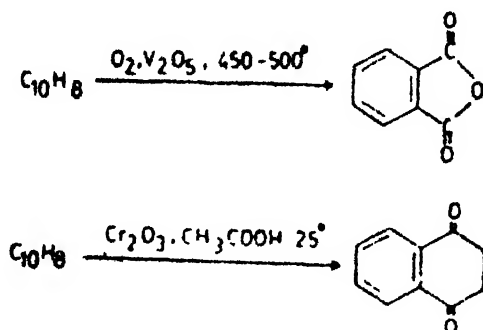
12.9.6 Structure of Naphthalene

The structure of naphthalene has been assigned based on the following pieces of evidence.

1. From elemental analysis and molecular weight determination, the molecular formula is found to be $C_{10}H_8$.
2. The molecular formula suggests that it is unsaturated like benzene, but it does not respond to Baeyer's test or decolorize bromine solution in CCl_4 . It can be fully reduced to decalin ($C_{10}H_{18}$) by absorption of 5 moles of hydrogen. It, therefore, contains five double bonds.
3. Naphthalene, in many of its chemical properties, closely resembles benzene.
 - a. It undergoes halogenation, nitration and sulfonation.

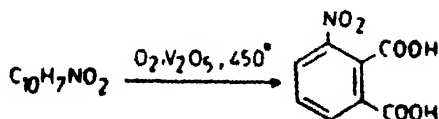
- b. Its amino derivative can be diazotized
 c. Naphthols give coloration with ferric chloride similar to phenol. These properties indicate the presence of one or more benzene rings in naphthalene.

On vigorous oxidation naphthalene is converted to phthalic anhydride, but under milder conditions it forms 1,4-naphthaquinone

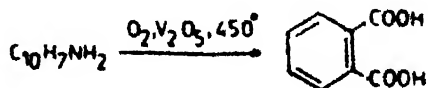


These reactions indicate the fusion of two cyclic structures at the *ortho* positions.

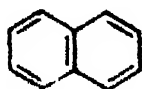
1-Nitronaphthalene, on vigorous oxidation yields 3-nitrophthalic acid, i.e., the benzene ring containing the $-\text{NO}_2$ group (electron deficient)



remains intact. 1-Aminonaphthalene, on the other hand, forms only phthalic acid, i.e., the benzene ring with high electron density is destroyed.



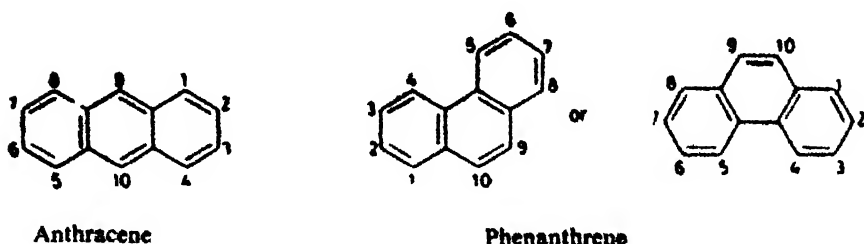
On the basis of these oxidation reactions it is concluded that naphthalene contains two benzene rings fused together at the *ortho* positions and its structure may be written as:



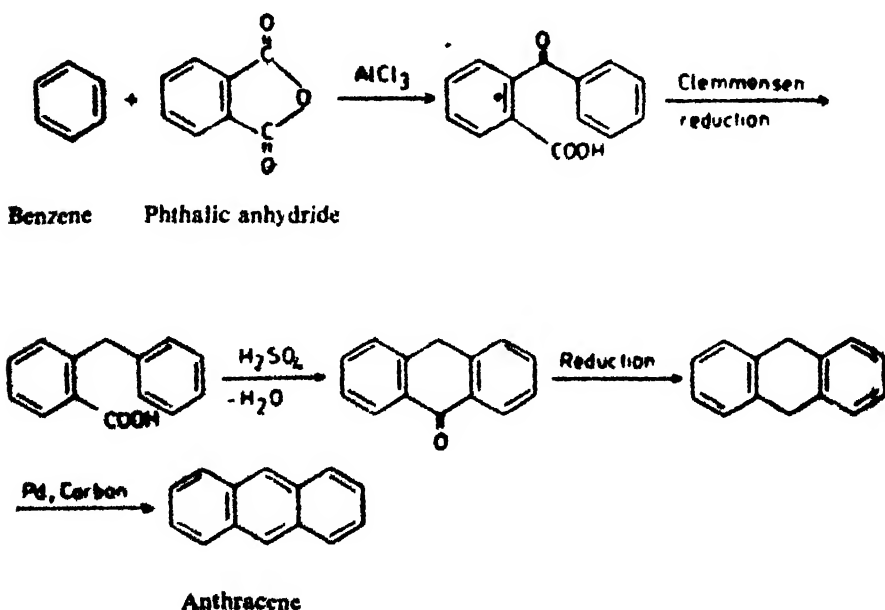
This structure has been confirmed by its independent synthesis due to Haworth.

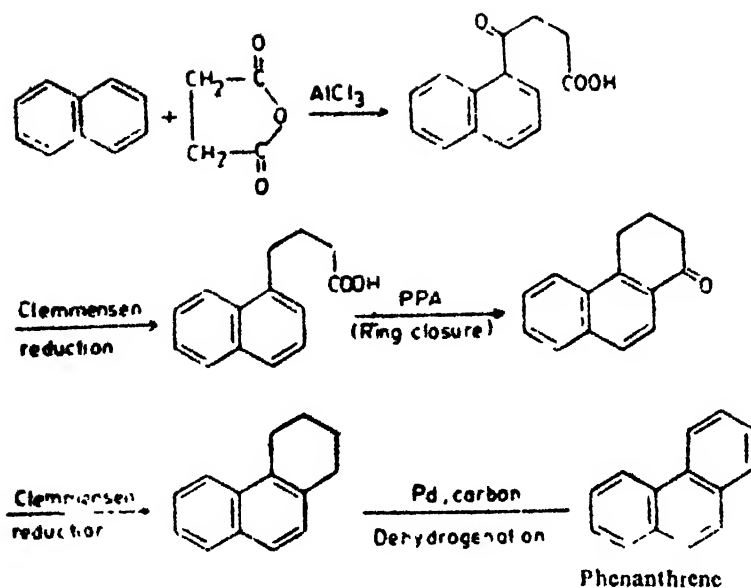
12.10 ANTHRACENE AND PHENANTHRENE

The two title compounds are isomeric hydrocarbons with the molecular formula $C_{14}H_{10}$. They contain three benzene rings fused together in the manner shown below. Anthracene (resonance energy 84 kcal/mole) is approximately 7 kcal/mole less stable than phenanthrene (resonance energy 91 kcal/mole).

**12.10.1 Preparation**

Synthesis of these two hydrocarbons can be accomplished in the laboratory in the following steps:

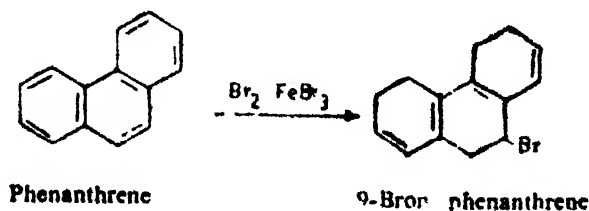
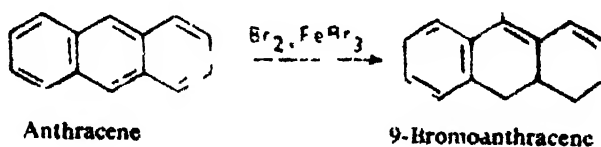




12 10.2 Reactions

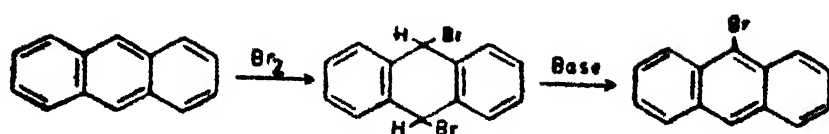
These two compounds undergo the following chemical reactions

1 *Electrophilic Reactions*: a Bromination of anthracene or phenanthrene takes place at the 9-position

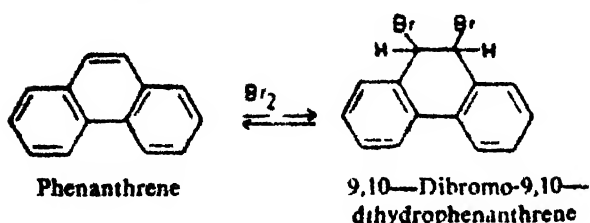


The attack at the 9-position is favored because the aromatic sextets are preserved in two of the three benzene rings in the intermediate carbonium ion in both these hydrocarbons. The attack at position —10 may also occur for the same reason.

There is also a tendency for addition to take place in both of these hydrocarbons, particularly phenanthrene.



Anthracene

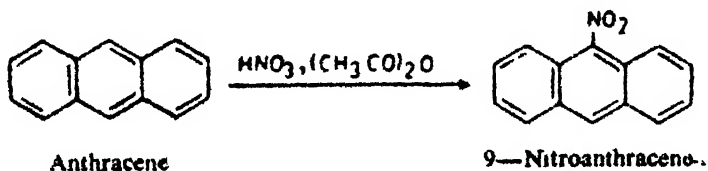


Phenanthrene

9,10—Dibromo-9,10—
dihydrophenanthrene

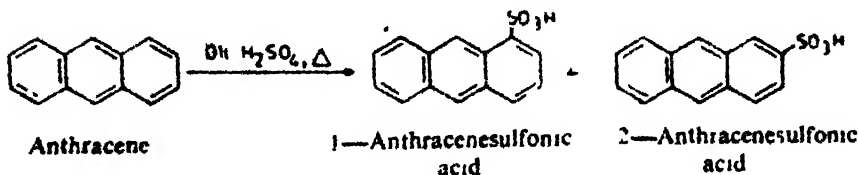
Chlorination of anthracene in CS_2 also leads to the introduction of chlorine at position-9.

b. Nitration takes place at the 9-position, while sulfonation yields a mixture of 1- and 2-isomers.



Anthracene

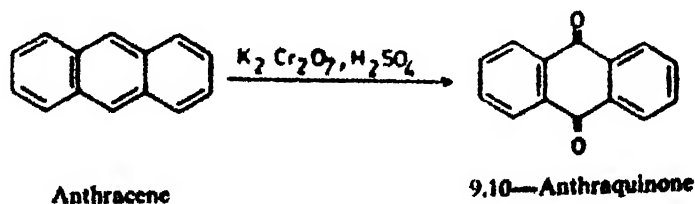
9—Nitroanthracene.



Anthracene

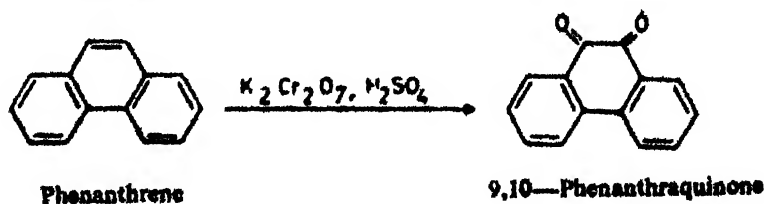
1—Anthracenesulfonic
acid2—Anthracenesulfonic
acid

2. **Oxidation:** Both the hydrocarbons are less resistant towards oxidation than naphthalene and readily form 9,10-quinones on oxidation with potassium dichromate in sulfuric acid.



Anthracene

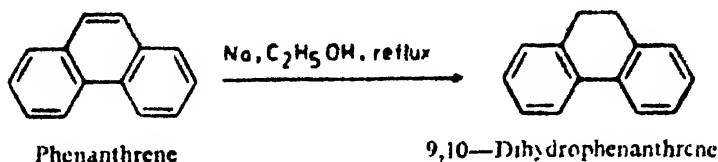
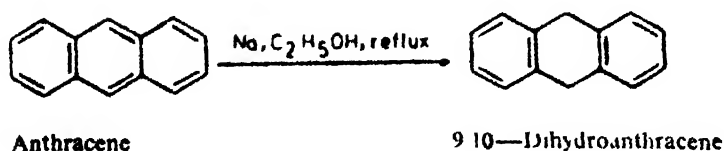
9,10—Anthraquinone



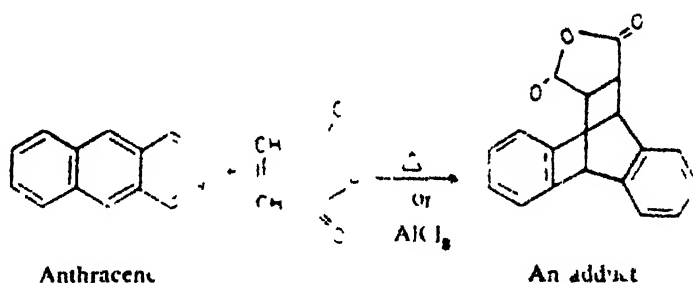
Phenanthrene

9,10—Phenanthraquinone

3. **Reduction:** Sodium in ethanol reduces these compounds to 9,10-dihydro derivatives.



4. **Diels-Alder Reaction:** The 9, 10-positions are very reactive in anthracene because it undergoes the D-A reaction with maleic anhydride in 99% yield, anthracene acts as a diene and adduct formation occurs at the 9, 10-carbon atoms.

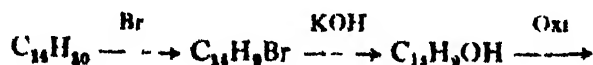


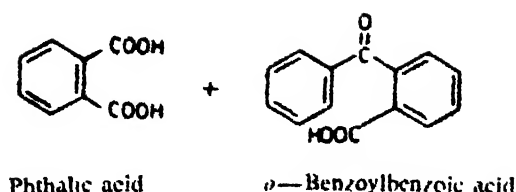
This method can be used to purify anthracene. The adduct is recrystallized and then decomposed to obtain pure anthracene.

12.10.3 Structure of Anthracene

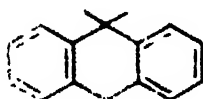
The structure of anthracene has been deduced from the following information:

1. From analytical data and molecular weight determination the molecular formula of anthracene is obtained to be $\text{C}_{14}\text{H}_{10}$.
2. Naphthalene undergoes halogenation, nitration and sulfonation like benzene and naphthalene which suggests that it is related to these hydrocarbons.
3. On bromination anthracene forms mono bromo anthracene ($\text{C}_{14}\text{H}_9\text{Br}$) which on fusion with KOH yields hydroxyanthracene ($\text{C}_{14}\text{H}_9\text{OH}$). This latter compound on vigorous oxidation affords phthalic acid and a small amount of *o*-benzoylbenzoic acid

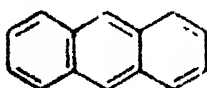




This confirms the presence of two benzene rings in anthracene and a skeleton of the following type.



This skeleton accounts for 14C atoms and in order to accommodate 10H it is evident that there should be three rings in anthracene. The central ring should have 2H atoms to give the structure of anthracene as represented below:



4. This structure has already been confirmed by its independent synthesis

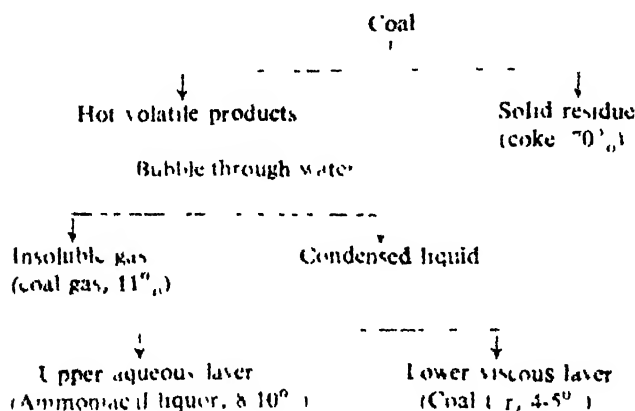
12.11 COAL TAR*

Coal is a rock derived from wood and other plant tissues that flourished several hundreds of million years ago. Although coals are sometimes described as form of carbon, this is not strictly true, they are usually intricate mixtures of complex compounds of carbon. Coals differ from one another in composition and properties. Coal tar is a heavy dark liquid containing a complex mixture of organic compounds. It is obtained by the destructive distillation or carbonization (1000-1400°C) of coal. The primary product of carbonization of coal is coke while the secondary products are coal tar, heavy oil, ammonia liquor and coal gas. Coal tar has been shown to contain approximately 93% of carbon, 4.5% of hydrogen and small amounts of nitrogen, oxygen and sulfur. It is a principal source of aromatic compounds of all types and more than 300 of them have been isolated.

The process of obtaining of coal tar involves thermal decomposition of coal together with distillation. When coal is heated in a temperature range

*Excessive contact of skin with coal tar is harmful as it may cause cancer because of the carcinogenic compounds that it contains.

of $500-750^{\circ}$ it is called *low temperature carbonization* and when heated above 1000°C it is *high temperature carbonization*. The interest in low temperature carbonization centers chiefly as the amount of tar produced in this case is 3-5 times more than that obtained from high temperature carbonization. Furthermore, coke obtained in low temperature carbonization is used as smokeless fuel for home heating purposes. A large variety of compounds decompose at high temperature and collect as a mixture called *coal tar* as shown in the schematic diagram below



The gaseous products are termed as *coal gas* and the residue which is predominantly carbon is known as *coke*, it finds use in the steel industry. Most of the coal tar produced in India is used either to make road tar or burnt as fuel in the steel industry.

Fractional Distillation of Coal Tar The constituents of coal tar are separated by fractional distillation. These are then purified according to need. The properties and composition of coal tars are materially influenced by the type of coal carbonized, the reaction temperature to which the tar vapors are exposed and the time of exposure. The primary products consist mainly of paraffin hydrocarbons, olefins, naphthalene, phenols and a wide variety of secondary products. Chemical changes usually described as cracking and polymerization also occur during distillation and the greater these changes, the lower the yield of oils distilling below 350° and the higher the yield of residual pitch. Typical fractions taken in a continuous coal tar distillation are given below:

1. **Light Oil or Crude Naphtha (up to 200°):** It is the first fraction. It is washed with cold sulfuric acid to remove pyridine and other basic materials, used in the synthesis of rubber, chemicals and in dyeing industry; and then with dil. sodium hydroxide to remove phenol, cresol, xylol, etc., and finally with water. It is then subjected to redistillation to obtain the following refined products:

a. 90° : *Benzol* ($90-110^{\circ}$): Compounds distilling below 90° constitute carbon disulfide, cyclopentadiene, etc. Cyclopentadiene is used in the manufacture of insecticides like aldrin and dieldrin. The 90% benzol fraction consists of benzene and toluene but predominantly (70%) of the former.

b. 50% *Benzol* ($110-140^{\circ}$): Half of this fraction ($\sim 45\%$) contains benzene along with toluene and xylene

c. *Solvent Naphtha* ($140-200^{\circ}$): It contains xylene and mesitylene. These hydrocarbons are used in dry cleaning, as solvents, dyes, in the drug and perfume industry and in timber preservation.

2. *Naphthalene Oil* ($200-250^{\circ}$): The fraction contains naphthalene and phenol. On cooling naphthalene (m.p. 80°) crystallizes out and is separated by centrifuging. It is then purified by sublimation. It is used in the manufacture of dyes, explosives, and phthalic anhydride. The mother liquor is treated with caustic soda followed by dil. sulfuric acid to regenerate phenol which is used extensively in plastic and resin industry.

3. *Heavy Oil* ($250-300^{\circ}$): No other chemicals are isolated from this fraction. Most of the oil is creosote blends.

4. *Anthracene Oil* ($300-350^{\circ}$): Principal constituents of this fraction are anthracene ($12-25\%$) and phenanthrene ($20-35\%$). These are used in the dye industry. The residue of this distillation is the coal tar pitch.

5. *Pitch*: This is the black residue left after the distillation of tar and is called *pitch*. It exhibits changes in viscosities with changes in temperature. Its properties can be modified by the addition of oils or solvents or by further polymerization. It finds minor uses in binders, adhesives and protective coatings in the shipping industry.

Creosote: Coal tar distillation produces, as part of the operation, a number of residual oils, namely naphthalene, drain oil, wash oil, heavy oil, etc. and creosote is one of the heavy tar oils. It is used to protect objects such as telephone poles and railroad tracks.

Road Tar: Road tar is generally made by mixing soft or medium pitch with a mixture of wash oil and heavy oil of required viscosity according to the Bureau of Indian Standard requirements.

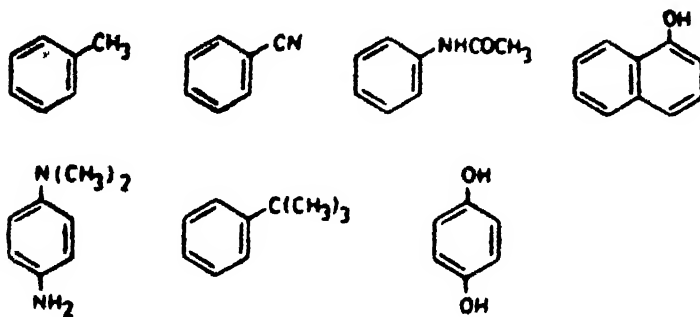
QUESTIONS

- 12.1 Arrange the following compounds in order of decreasing reactivity towards electrophilic substitution:

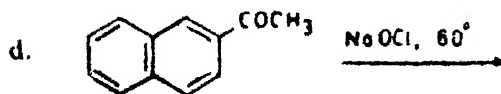
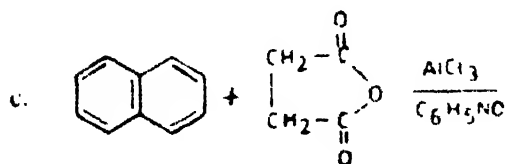
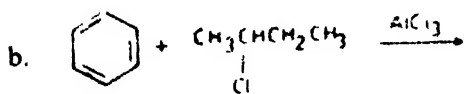
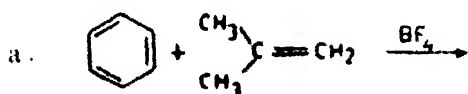


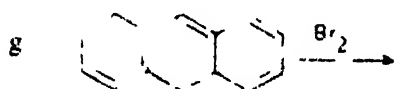
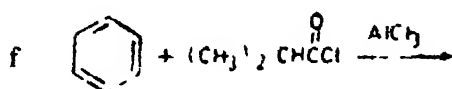
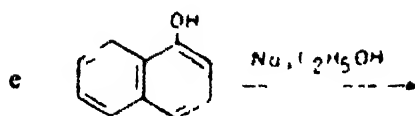
- 12.2 Draw all the possible structures of the aromatic compounds with the formula C_8H_{10} containing a benzene ring.

- 12.3 If the rings of each of the following compounds were nitrated where would you expect the nitro group to enter (there may be more than one positions):

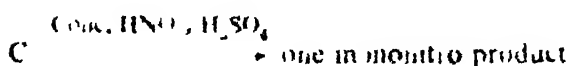
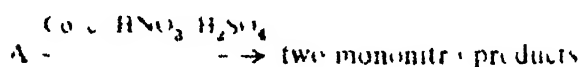


- 12.4 Write a mechanism for the chlorination of benzene in the presence of AlCl_3 as catalyst.
- 12.5 Explain with the help of a potential energy diagram how sulfonation of naphthalene under different conditions can lead to different products. Label the appropriate features of the diagram.
- 12.6 Complete the following reactions:



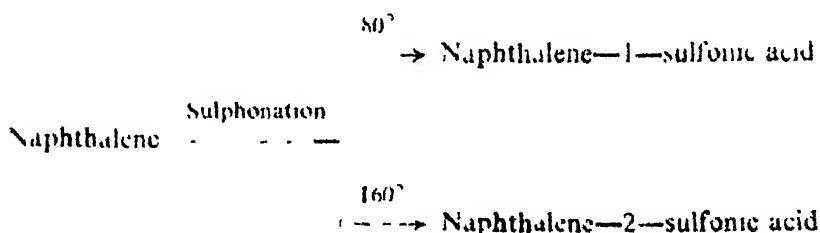


- 12.7 Compounds A, B and C are three isomeric derivatives of benzene. Identify which is *ortho*, *meta* or *para* from the products of nitration.



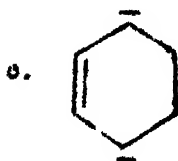
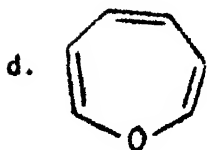
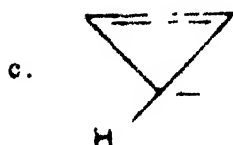
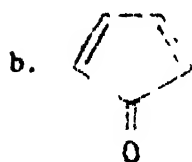
- 12.8 Describe the necessary conditions and reagents required to convert benzene into the following:
Nitrobenzene, ethylbenzene, cyclohexane, benzaldehyde, chlorobenzene, *t*-butylbenzene, acetophenone and benzoic acid.
- 12.9 Would you expect *m*-dinitrobenzene to undergo bromination with a halogen carrier rapidly or slowly? Why?
- 12.10 A hydrocarbon (A) of molecular formula C_8H_{10} adds chlorine to give (B), $\text{C}_8\text{H}_{10}\text{Cl}_2$. Hydrolysis of (B) gives (C), $\text{C}_8\text{H}_{12}\text{O}_2$. Oxidation of (C) gives two acids which are identified as benzoic acid and acetic acid. Explain the reactions.
- 12.11 Compound (A), C_8H_{10} yields two mononitro nuclear substitution products (A), on oxidation yields (B), $\text{C}_7\text{H}_6\text{O}_4$ which also gives two

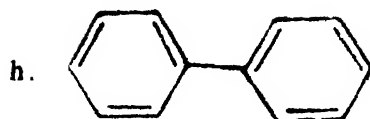
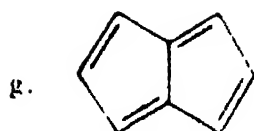
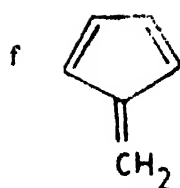
- mononitro nuclear substitution products. Write the structure of (A) and explain the reactions.
- 12.12 How will you convert naphthalene into:
(i) Anthranilic acid and (ii) 2-Naphthyl-1, 2-propanol
- 12.13 a. State Hückel rule. How can it be used to justify the aromatic character of benzene, naphthalene and anthracene?
b. How are the relative positions of the methyl group in different xylenes established?
- 12.14 How will you prepare naphthols from naphthalene? What is the action of chlorine on naphthalene?
- 12.15 How do you account for the fact that phenol is more easily attacked by electrophilic reagents than nitrobenzene?
- 12.16 Discuss the structure of benzene in terms of orbital and resonance concepts
- 12.17 How is anthracene prepared? Discuss its properties and uses. How is alizarin obtained from it?
- 12.18 a. State the evidence on which the structure of naphthalene is based.
b. How are β -naphthol, α -nitronaphthalene and β -naphthalene-sulfonic acid prepared?
- 12.19 Explain the experimental observation reported below:



- 12.20 Compound A and B are isomers having the formula C_8H_{10} . On oxidation A gives benzoic acid while B gives phthalic acid which forms an anhydride C on heating. Write down the names and structural formulas of A, B and C. Explain the reactions involved.
- 12.21 Establish the structure of benzene.
- 12.22 Discuss the constitution of naphthalene.
- 12.23 Nitration of toluene is easier than that of benzene. Explain.
- 12.24 a. How is benzene obtained from coal tar?
b. How does benzene react with the following?
(i) Conc. H_2SO_4 (ii) Chlorine, $AlCl_3$ (iii) Conc. HNO_3 , H_2SO_4 .
- 12.25 a. What do you understand by electrophilic substitution in the benzene ring?
b. Discuss the orienting influence of the following groups on substitution in aromatic compounds by electrophilic reagents:
 $-NH_2$, $-NO_2$, $-Cl$.

- 12.26 What do you understand when one says that the cyclopentadiene anion is aromatic?
- 12.27 Halogens in halobenzenes are deactivating but *ortho*- and *para* directing in electrophilic substitution. Explain.
- 12.28 Offer explanation for the following observations:
- Toluene requires lower temperature (30°) than benzene (55°) for nitration.
 - Chlorobenzene is less reactive than benzene.
 - t*-Butylbenzene is more reactive than toluene towards electrophilic substitution.
 - The C_1-C_2 bond distance in naphthalene is shorter than C_2-C_3 bond.
 - Nitrobenzene is used as a solvent in certain Friedel-Crafts acylations
 - Aniline does not undergo the Friedel-Craft reaction though $-NH_2$ group is electron-donating.
- 12.29 What do you understand by aromaticity? Which of the following structures would be aromatic? Explain.





12.30 Make the following conversions:

- Benzene to benzamide
- Benzene to *p*-bromobenzyl chloride
- Ethylbenzene to *p*-bromostyrene
- Benzene to *m*-nitrochlorobenzene
- Toluene to benzonitrile

Organic Halogen Compounds

Section A: ALKYL HALIDES

Halogen containing organic compounds are called halogenoalkanes. They have the general formula $C_nH_{2n+1}X$ or RX where R is any alkyl group and X represents a halogen atom F , Cl , Br or I . These compounds undergo a wide variety of reactions and constitute one of the most important intermediates in organic syntheses. Very few organic halides occur in nature and they thus do not pose a serious environmental problem. A majority of the halides are employed as insecticides and there exists virtually no micro-organism which can degrade them into non-toxic metabolic products.

13.1 NOMENCLATURE

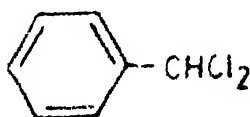
Organic halides may be according to trivial or IUPAC system of nomenclature. In trivial nomenclature simple alkyl halides are usually named as alkyl derivatives of the corresponding halogens. The name of the alkyl group precedes the name of the halide.



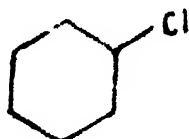
Methyl chloride



n-Butyl bromide



Benzal chloride

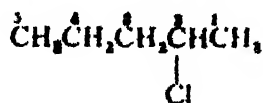


Cyclohexyl chloride



3-Fluorocyclopentene

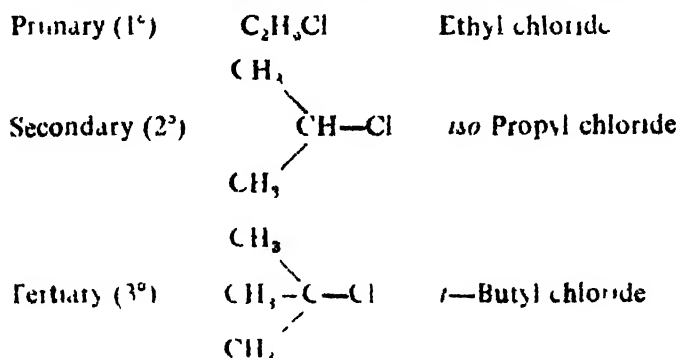
According to the IUPAC system the compound is named as a halogen derivative of a parent hydrocarbon, i.e., as haloalkane. The chain is numbered to give the halogen the lowest possible number. In writing the name the halogen is attached as a prefix (*fluoro*, *chloro*, *bromo* or *iodo*) together with a number indicating the position of attachment to the carbon chain.



2-Chloropentane



Alkyl halides may be classified into primary, secondary and tertiary depending on the number of alkyl groups linked to the central carbon atom



13.2 PHYSICAL PROPERTIES OF ALKYL HALIDES

The alkyl halides are insoluble in water though they are more polar than alkanes. They cannot form H—bond with water and are thus insoluble but are soluble in organic solvents as are the corresponding alkanes. As a class they are more dense than alkanes. Polyhalogenated compounds have higher boiling points than alkanes of the corresponding carbon chain. For a given alkyl group the boiling point increases with the increasing atomic weight of the halogen.

R	F	Cl	Br	I
CH_3	78.4	24.2	36	42.4
$-\text{CH}_2\text{CH}_3$	37	12.3	38.4	72.3
$\text{CH}(\text{CH}_3)_2$	25	46.6	71.0	102.5

A fluoride is the lowest boiling compound while an iodide is the highest. The C—X bond distance increases in going from fluorine to iodine because the higher halogens are substantially larger than the lower ones.

Compound	C—X (Å)
CH_3F	1.385
CH_3Cl	1.784
CH_3Br	1.939
CH_3I	2.139

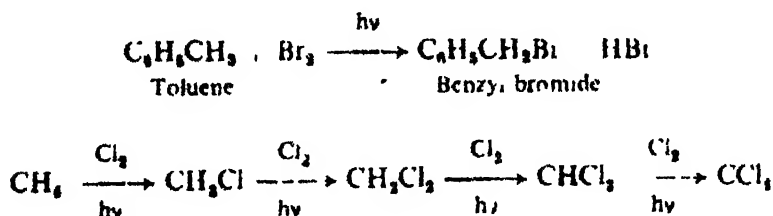
The C—X bond is polar because a halogen is more electronegative than carbon and the dipole moments of the various methyl halides have the following values:

Compound	μ_D
CH_3F	1.82
CH_3Cl	1.94
CH_3Br	1.79
CH_3I	1.64

13.3 PREPARATION OF ALKYL HALIDES

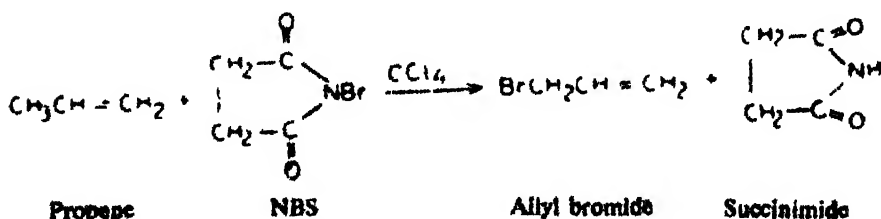
Alkyl halides may be prepared in the laboratory by the following general methods.

1. *Halogenation of Hydrocarbons*: Chlorine or bromine replaces hydrogen in aliphatic and alicyclic hydrocarbons. Preparation of organic halides by free radical halogenation of hydrocarbons in the presence of uv light or peroxides as catalyst is an important industrial method. In the laboratory organic halides are obtained photochemically. Reaction of



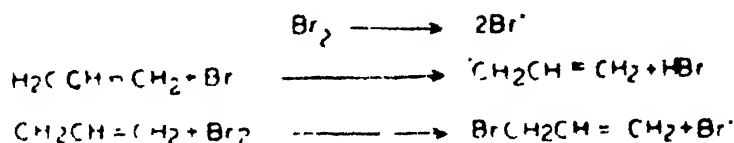
chlorine with methane proceeds to form carbon tetrachloride in the presence of sun-light. Chloroform is usually stored in tightly capped amber bottles and is mixed with 1% ethyl alcohol to discourage the formation of phosgene (COCl_2), a highly toxic gas.

Hydrocarbons containing allylic carbon chain can alternatively be brominated by refluxing with N-bromosuccinimide (NBS) in the presence of benzoyl peroxide, which acts as a radical initiator,

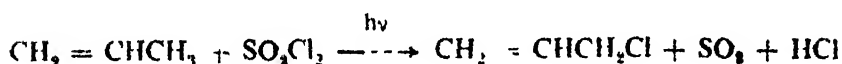
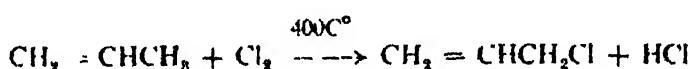


Mechanism:

N-Bromosuccinimide is insoluble in CCl_4 but it provides a constant but very low concentration of bromine by reacting with HBr formed in the substitution reaction.

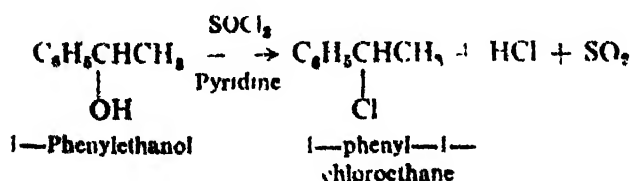
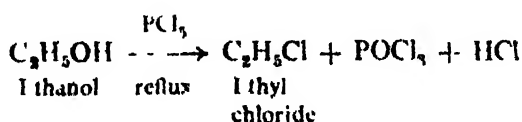
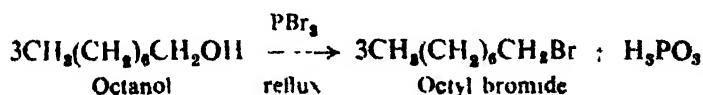


Allylic chlorination may be effected by the following methods

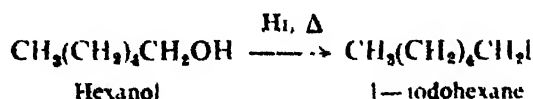


Fluoro hydrocarbons cannot be prepared by direct fluorination of alkanes because an explosive reaction takes place

2 **From Alcohols:** Another important method of synthesizing organic halides utilizes alcohols as the starting material. Various reagents such as PCl_5 , PBr_3 and SOCl_2 form halides by replacing the $-\text{OH}$ group.

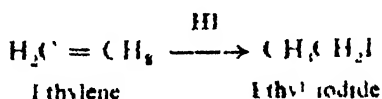


The three hydrohalogen acids HI, HBr and HCl also react with alcohols but at different rates, i.e. $\text{HI} > \text{HBr} > \text{HCl}$

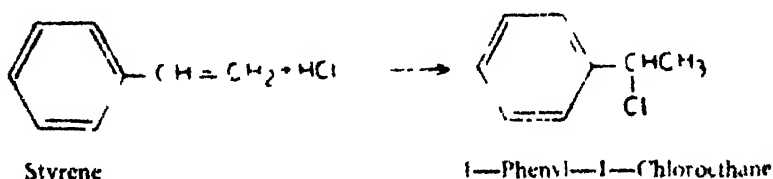


With primary alcohols hydroiodic acid reacts most readily while hydrochloric acid requires zinc chloride as a catalyst and hydrobromic acid displays an intermediate reactivity. Furthermore a tertiary alcohol reacts more rapidly than a secondary which in turn reacts faster than a primary alcohol.

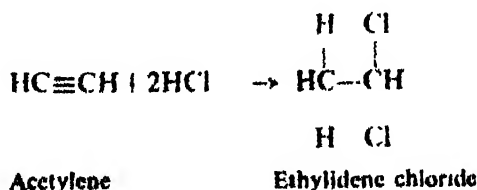
3. *Addition of Hydrogen Halides to Alkenes and Alkynes* A halogen can be introduced into an alkene or alkyne by the addition of a hydrogen halide to form an organic halide. This also constitutes an industrial method for their manufacture.



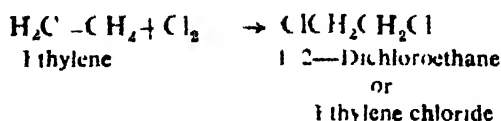
In the case of unsymmetrical olefins the reaction proceeds in accordance with Markownikoff's rule. The reaction of hydrogen halides with alkynes



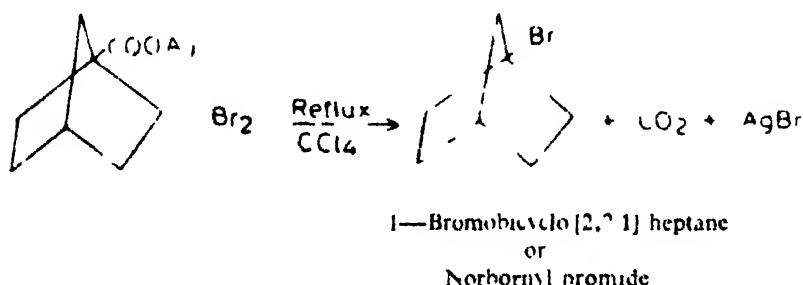
yields vicinal halides.



4 *Addition of Halogens to Alkenes* Dihalides are formed by the addition of halogens to alkenes

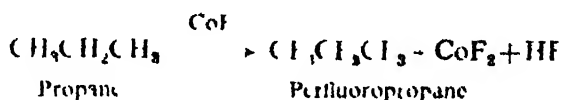


5 *Hunsdiecker Reaction* This method requires refluxing of the silver salt of the carboxylic acid with bromine in CCl_4 . It is particularly useful for preparing bridgehead halides because the reaction proceeds via a free radical and a bridgehead free radical has been shown to be possible.

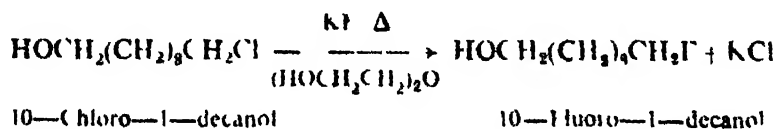


The yields in this reaction are usually low.

6 *Fluorination of Hydrocarbons* Reaction of hydrocarbons with elemental fluorine is unsatisfactory as it replaces all the hydrogen atoms.



A single fluorine may replace chlorine by heating an aliphatic chloride with KI in diethylene glycol.

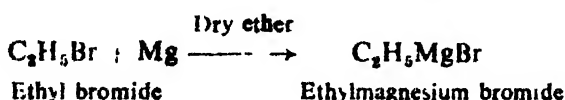


13.4 REACTIONS OF ALKYL HALIDES

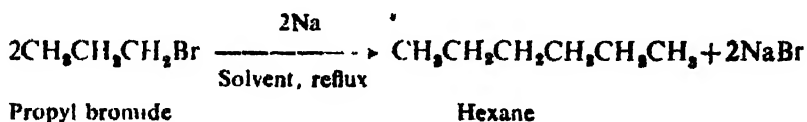
1 One of the most important and widely investigated reactions of alkyl halides is nucleophilic substitution. The halogen atom can be displaced by a variety of nucleophilic reagents to form useful products. Some representative examples are given below.

	OH^-	\rightarrow	ROH	(alcohol)
	OC_2H_5^-	\rightarrow	ROC_2H_5	(ether)
	OAc^-	\rightarrow	ROAc	(ester)
	CN^-	\rightarrow	RCN	(cyanide)
	NH_3^-	\rightarrow	RNH_2	(primary amine)
	SH^-	\rightarrow	RSH	(thioalcohol)
	$\text{HC}\equiv\text{C}^-\text{Na}^+$	\rightarrow	$\text{RC}\equiv\text{C}-\text{R}$	(alkyne)
	$\text{C}_6\text{H}_5\text{O}^-$	\rightarrow	ROC_6H_5	(ether)
RX	$\text{Ag}-\overset{\text{O}}{\overset{+}{\text{N}}}-\text{O}^-$	\rightarrow	$\text{R}-\overset{\text{O}}{\overset{+}{\text{N}}}-\text{O}^-$	(nitroparaffin)
	$\text{C}_2\text{H}_5\text{NH}_2$	\rightarrow	$\begin{array}{c} \text{C}_2\text{H}_5 \\ \diagdown \\ \text{NH} \\ \diagup \\ \text{R} \end{array}$	(secondary amine)
	N_3^-	\rightarrow	RN_3	(azide)
	$\begin{array}{c} \text{CN} \\ \diagup \\ \text{CH}^- \\ \diagdown \\ \text{COOC}_2\text{H}_5 \end{array}$	\rightarrow	$\begin{array}{c} \text{CN} \\ \diagup \\ \text{RCH} \\ \diagdown \\ \text{COOC}_2\text{H}_5 \end{array}$	(cyanoacetic ester)
	$\begin{array}{c} \text{COOCH}_3 \\ \diagup \\ \text{CH}^- \\ \diagdown \\ \text{COOCH}_3 \end{array}$	\rightarrow	$\begin{array}{c} \text{COOCH}_3 \\ \diagup \\ \text{RCH} \\ \diagdown \\ \text{COOCH}_3 \end{array}$	(substituted malonic ester)

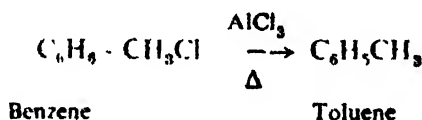
2. *Grignard Reagents*: Alkyl halides form Grignard reagents on treatment with magnesium in dry ether which find their own series of uses in synthetic organic chemistry. Thus ethylmagnesium bromide is obtained by refluxing ethyl bromide with magnesium turnings in ether.



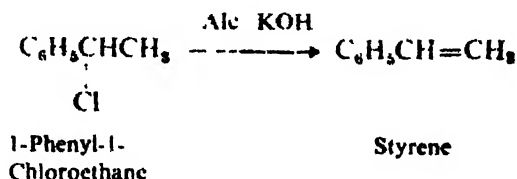
3 *Wurtz Reaction*: Symmetrical paraffinic hydrocarbons may be prepared by treating alkyl halides with sodium and refluxing in a suitable solvent.



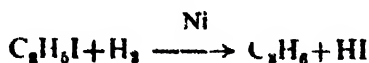
4 *Friedel Crafts Reaction*. An alkyl side chain can be attached to an aromatic ring by the Friedel-Crafts reaction.



5. *Dehydrohalogenation*: In the presence of an alcoholic solution of KOH, HX is eliminated from an organic halide to form an unsaturated product.



6. *Reduction*: Organic halides are reduced to hydrocarbons in the presence of hydrogen and Ni as catalyst.



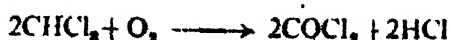
7. *Reaction with HNO₃*: Chloroform with nitric acid forms chloropicrin.



Chloroform on boiling with aq. sodium hydroxide solution forms sodium formate.



Oxidation (exposure to air and sun light) of chloroform converts it into a poisonous gas phosgene.



13.5 USES OF ALKYL HALIDES

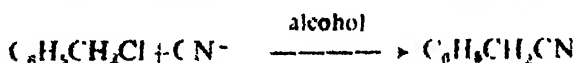
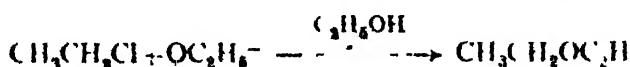
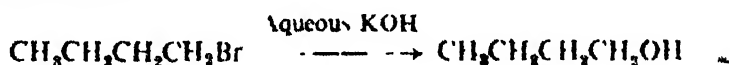
Chlorinated hydrocarbons are very good solvents for non-polar material. Methylene chloride and chloroform dissolve old paints. Carbon tetrachloride is used in dry cleaning as it dissolves oil and grease. Freon (CCl_2F_2) a fluorocarbon is used as a refrigerant fluid. It is a non-toxic liquid.

13.6 MECHANISM OF NUCLEOPHILIC SUBSTITUTION REACTIONS

A substitution reaction may be described as one in which a substituent is replaced by another. A nucleophile (Y^-) attacks the carbon atom bearing the group to be replaced called the leaving group (L). It may be depicted as follows:



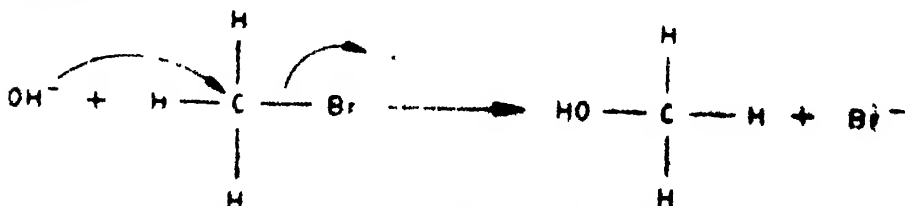
The leaving group departs with its pair of bonding electrons. Some examples are described below:



These reactions have been classified into two types called $\text{S}_{\text{N}}1$ and $\text{S}_{\text{N}}2$ by Ingold and Hughes.

13.6.1 The $\text{S}_{\text{N}}2$ Reaction

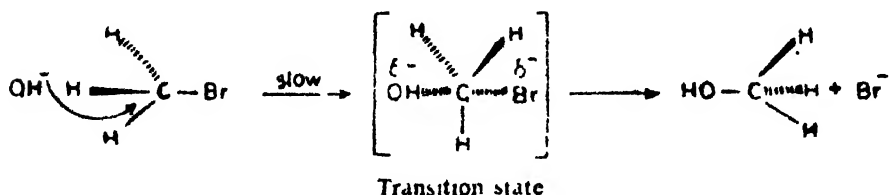
The bimolecular reaction is designated $\text{S}_{\text{N}}2$. Consider the reaction between a primary alkyl halide, methyl bromide and hydroxide ion to form methyl alcohol.



The reaction takes place by a collision between the hydroxide ion and methyl bromide molecule, therefore, the rate should depend on the concentration of both these reagents. This is found to be so and the reaction complies with the following rate equation.

$$\text{Rate} = k_2[\text{CH}_3\text{Br}][\text{OH}^-]$$

In other words, it is a second order reaction, i.e., both the reactants are involved in the slow step of the reaction. The mechanism of the reaction may be formulated as follows:



The hydroxide ion attacks the carbon atom bearing the leaving group from the backside and the bromide ion departs from the opposite side. At the transition state both the OH^- and Br^- ions are only partially bonded to the central carbon atom which attains a coplanar configuration. The final result is the formation of a new covalent bond between the hydroxide ion and the carbon atom with the loss of the bromide ion.

Energy must be supplied to the reactants before they reach the transition state and the greater the amount of energy that must be supplied to the system in order for the reaction to take place, the slower is the rate of the reaction.

It has been observed in an $\text{S}_{\text{N}}2$ reaction that if we start with an optically active organic halide of known stereochemistry and optical rotation, the

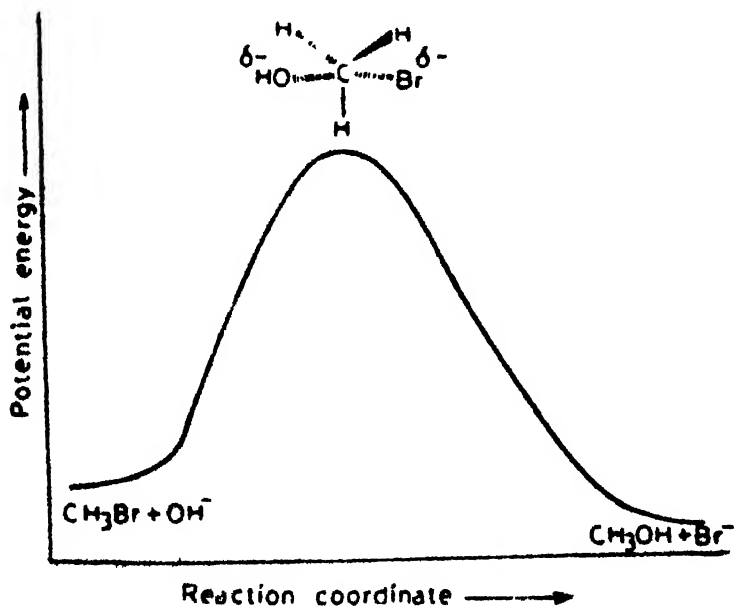
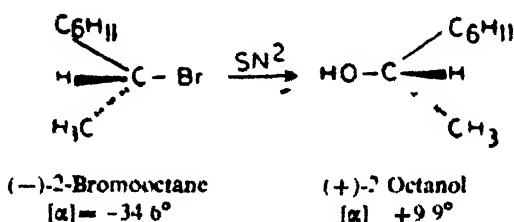


Fig. 13.1 Potential energy diagram for an $\text{S}_{\text{N}}2$ process

product obtained has the opposite configuration. Thus (–)-2-bromooctane, $[\alpha] = 34.6^\circ$ (100% optical purity) on reaction with sodium hydroxide forms (–)-2-octanol, $[\alpha] = 9.9^\circ$ (also 100% optical purity):



The enantiomer of 2-octanol has an optical rotation of $[\alpha] = -9.9^\circ$. This result indicates that pure 2-octanol of opposite rotation is obtained and hence there has been no loss in optical activity. The hydroxyl ion thus does not occupy the same position vacated by the bromide ion. The change in configuration may be pictured as the molecule turned inside out like an *umbrella in a storm*. The reaction as a result proceeds with inversion of configuration. This stereochemistry thus indicates that the nucleophile makes a rear attack in an $\text{S}_\text{N}2$ substitution and expels the leaving group from the front. The result of such an attack is to 'flip' the other three atoms or groups from one side of the carbon atom to the other. This process is known as 'Walden inversion'.

Usually a strong base will bring about this change more readily than a weaker one. There is, however, no parallelism between basicity and nucleophilicity, a relative base strengths of nucleophiles is $\text{I}^- < \text{Br}^- < \text{Cl}^- < \text{CH}_3\text{COO}^- < \text{CN}^- < \text{OH}^- < \text{OR}^- < \text{NH}_2^- < \text{CH}_3^-$. Among the halogens the basicity decreases in the order $\text{F}^- > \text{Cl}^- > \text{Br}^- > \text{I}^-$ but the nucleophilicity is reverse. Basicity is concerned with the extent of coordination of a base with a hydrogen atom while nucleophilicity pertains to the attack of a nucleophile at the carbon atom. For a nucleophilic reaction to be successful, a useful generalization is that the nucleophile must be significantly more basic than the departing group. The rate of an $\text{S}_\text{N}2$ reaction is independent of the polarity of the solvent.

Since a nucleophile attacks the central carbon atom from the backside, it is anticipated that the reactivity of an alkyl halide will be altered by a change in its structure. It is observed that replacement of hydrogen atoms for alkyl groups hinders the approach of the nucleophile and thus an $\text{S}_\text{N}2$ reaction is subject to steric hindrance. The reactivity of alkyl groups thus follows the order primary > secondary > tertiary, i.e., a tertiary halide is the least reactive in an $\text{S}_\text{N}2$ reaction. The effect of substitution on the $\text{S}_\text{N}2$ reactivity for the following reaction is given in which R is varied.

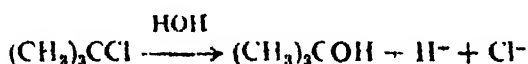


Compound	β -R	Relative Rate
$\text{CH}_3\text{CH}_2\text{Br}$	H, H, H	1.00
$\text{CH}_3\text{CH}_2\text{CH}_2\text{Br}$	CH_3 , H, H	0.28
$(\text{CH}_3)_2\text{CHCH}_2\text{Br}$	CH_3 , CH_3 , H	0.30×10^{-6}
$(\text{CH}_3)_3\text{CCH}_2\text{Br}$	CH_3 , CH_3 , CH_3	4.2×10^{-6}

Thus the $\text{S}_{\text{N}}2$ rate decreases enormously as the substitution at the β -position increases. A hindrance in the rate of a reaction when bulky groups are present in the vicinity of a reaction site is known as *steric hindrance*.

13.6.2 The $\text{S}_{\text{N}}1$ Reaction

The unimolecular reaction is abbreviated $\text{S}_{\text{N}}1$. In contrast to a primary halide, a tertiary halide viz. *t*-butyl chloride undergoes substitution to form *t*-butyl alcohol by a unimolecular process.

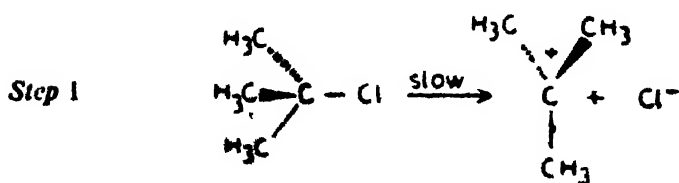


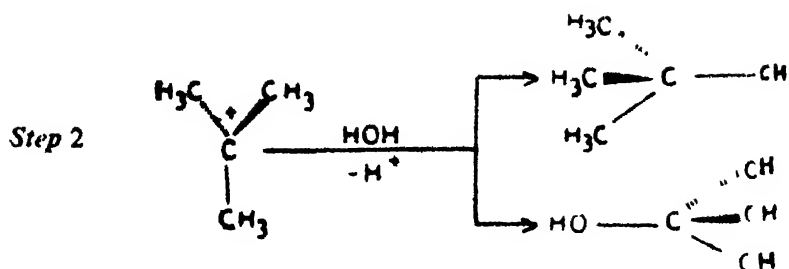
The rate of the reaction depends only on the concentration of the alkyl halide and is independent of the concentration of the added nucleophile. The $\text{S}_{\text{N}}1$ reaction thus follows the following rate equation:

$$\text{Rate} = k_1[(\text{CH}_3)_3\text{CCl}]$$

Since the nucleophile in this case is a molecule of the solvent this reaction is also called *solvolysis*.

The mechanism of the reaction must involve two steps. In the first step the halide ionizes to form an intermediate carbocation in a slow step which then readily combines with the solvent or the added nucleophile to form the products.





Although it might seem that the addition of a nucleophile, i.e., a OH^- ion would affect the rate of the reaction in step 2, but this step is so much faster than step 1 that the effective rate measured is that of step 1, i.e., the ionization step. The intermediate lies at a relative minimum on the potential energy diagram and the process will have two transition states as shown in Fig. 13.2. An intermediate is a species of relatively high energy content compared to the reactants.

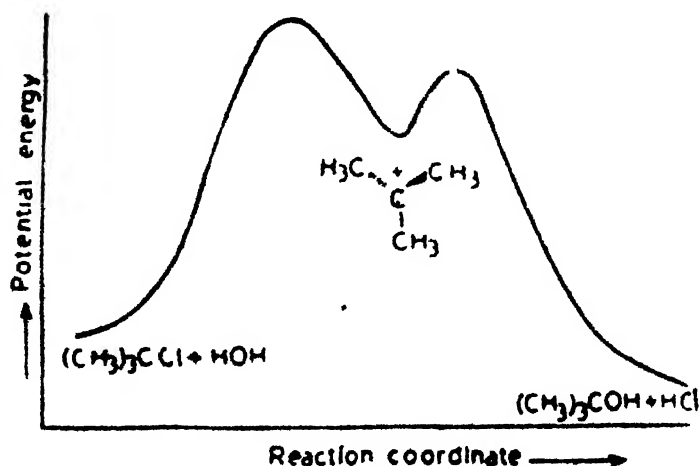
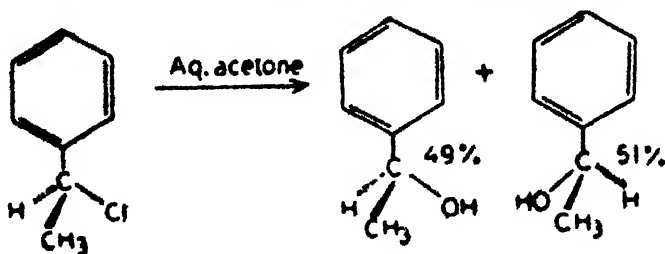


Fig. 13.2 Potential energy diagram for an $\text{S}_{\text{N}}1$ process

The stereochemistry of the $\text{S}_{\text{N}}1$ reaction is more complex than that of the $\text{S}_{\text{N}}2$ reaction. The $\text{S}_{\text{N}}1$ reaction of an optically active substance, say 1-phenyl-1-ethyl chloride proceeds with essentially complete racemization.

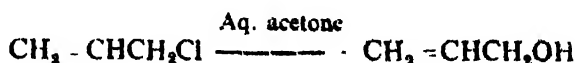


This may be rationalized from the structure of the intermediate. A carbocation is planar, i.e., sp^2 hybridized, therefore, the solvent molecules can attack it from either side to form the product. If the attack occurs from the opposite side of the original carbon-halogen bond then *inversion* results, if the attack occurs from the same side as the original carbon halogen bond, then the reaction is said to proceed with *retention*. In general a nucleophile may attack a carbon from either side with equal probability and thus give equal amounts of inversion and retention products. The reaction, therefore, proceeds with the *racemization* of the products. In the above example the asymmetry of pure 1-phenylethyl chloride is lost in forming the symmetrical intermediate. This reacts with the solvent to produce an equal amount of isomeric 1-phenylethanol and with the loss of resultant optical activity or racemic 1-phenylethanol. In summary, starting with an organic halide of known stereochemistry the product obtained is racemic, i.e. the product consists of a mixture of two enantiomers of equal and opposite optical rotation. This result serves as added confirmation of the S_N1 course for the reaction.

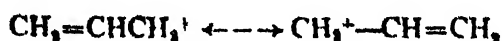
The rate-determining step of an S_N1 reaction is the formation of the carbocation. Therefore, the ease of the reaction will depend entirely on the stability of this ion. This, indeed, is true and the order of reactivity among organic halides decreases in the order: *tert* > *secondary* > *primary*. The primary alkyl halides seldom hydrolyze by S_N1 mechanism. Furthermore, since a polarization of the carbon-halogen bond takes place in the slow step, the alkyl halides display the following reactivity order: $RI > RBr > RCl > RF$. This order is the same for S_N2 reactions and is consistent with the bond strengths of the alkyl halides. The stability of the carbocation is affected by changes in the structure of the halide. Thus, the ionization of 1-chlorobicyclo [2.2.1] heptane is prevented by the geometry



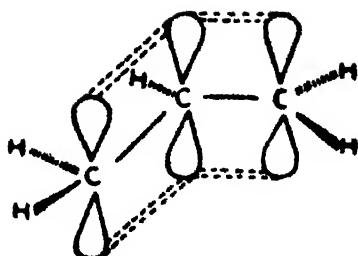
of the molecule. The carbocation, if produced, cannot attain a planar configuration; as a result the S_N1 reaction of this compound is extremely slow. In contrast allyl chloride shows a high reactivity.



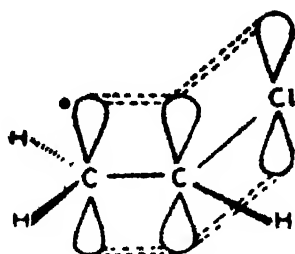
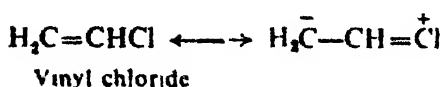
This reactivity is attributed to the stabilization of the intermediate allyl cation



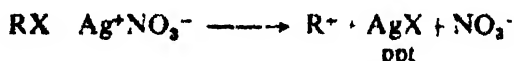
The molecular orbital representation of the cation looks as follows. Vinyl



chloride, on the other hand, does not undergo S_N2 displacement because of the π -orbital overlap of the double bond with a lone pair of the halogen atom to give a partial double bond character.



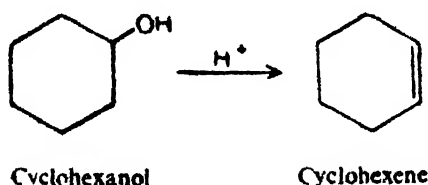
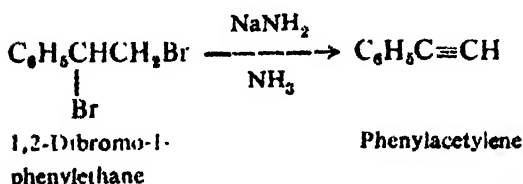
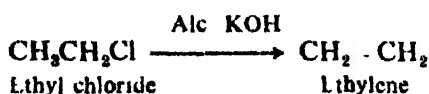
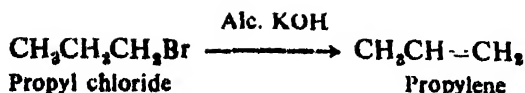
The ionization of the carbon-halogen bond is also influenced by the polarity of the solvent and S_N1 reactions are faster in more polar solvents such as water, alcohol, acetic acid, acetone, etc. The solvent molecules, due to solvation, stabilize both the anions and the cations. Water is probably the most effective solvent. A metal ion such as Ag^+ which has a strong affinity for halide ion exerts a powerful influence in the formation of a carbonium ion and thus enhances the rate of hydrolysis



Secondary halides lie on the border line and undergo substitution both by S_N1 and S_N2 mechanisms. One mechanism, however, may be excluded at the expense of the other by changing the experimental conditions. Thus strong nucleophiles favor S_N2 while weak bases favor S_N1 reaction: 2-chlorooctane reacts with a strong base (ethoxide ion) by the S_N2 process.

13.7 ELIMINATION REACTIONS

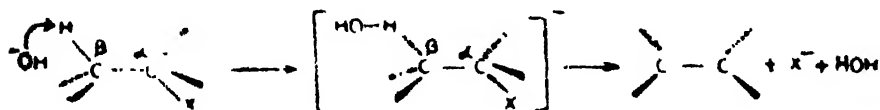
Alkyl halides have the tendency to produce more than one product in displacement reactions. Such products are obtained by the concurrent occurrence of another important class of reactions known as *elimination*. These reactions constitute a general method for the preparation of alkenes under appropriate conditions. In an elimination reaction two atoms or groups are lost from adjacent carbon atoms to yield products containing a C-C or a C=C bond. Some examples are cited below:



Two types of elimination reactions have been recognised and are designated E1 and E2 (E, stands for elimination).

13.7.1 Bimolecular Elimination (E2)

It is the most common of the elimination reactions and occurs by the action of a base on an alkyl halide with the formation of a C=C double bond. It is a second order reaction as the rate depends both on the concentration of the substrate and the base. In contrast to a displacement reaction, in an E2 reaction, a base abstracts a β -proton with the simultaneous displacement of the leaving group. The mechanism is depicted as follows:

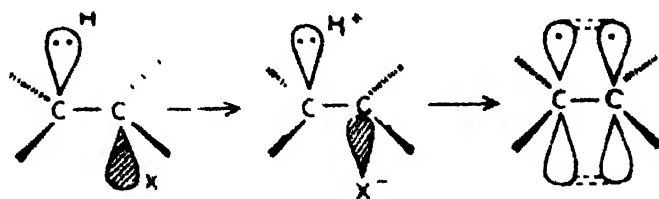


The dotted lines in the representation of the transition state indicate the bonds which are in the process of being broken or made. This process is also referred to as the β -elimination.

Since a base attacks the proton, therefore, strong bases accelerate elimination and strongly basic species like the sodium and potassium alkoxides are used. A weaker base such as an acetate ion would not lead to appreciable alkene formation. The structural features of the alkyl halide are also important in an E2 reaction, and an increase of alkyl substitution at the α -position favors elimination over substitution. It may be recalled that this order of

reactivity is the reverse to that for the S_N2 reaction. Furthermore, a larger acidity of the β -H and a high temperature are also conducive to E2 reaction.

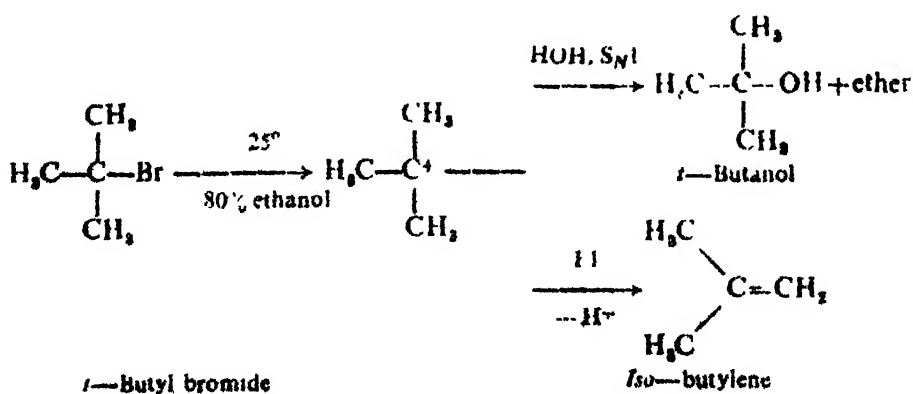
A *trans* elimination process in which the atoms leave from the opposite sides is observed in most cases. The reaction, in other words, is stereospecific. The reason for this may be that the bond orbitals of the two leaving



groups should be in the same plane, with the electrons of the orbital left behind being located at the rear of those departing with the anion as shown above.

13.7.2 Monomolecular Elimination (E1)

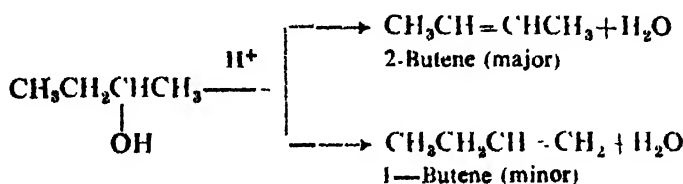
This reaction is particularly common in tertiary halides and takes place in the absence of a strong base. It is characterized by a first order kinetics and the rate is dependent only on the concentration of the substrate. This suggests a mechanism similar to the S_N1 process. The reaction occurs by a rate-controlling formation of a carbonium ion by the heterolysis of a C—halide bond in a polar solvent. The carbocation so formed has two pathways available to it to stabilize itself. It can either combine with the solvent to form a substitution product *via* the S_N1 -reaction or can lose β -proton to yield an alkene. This is illustrated for *t*-butyl bromide.



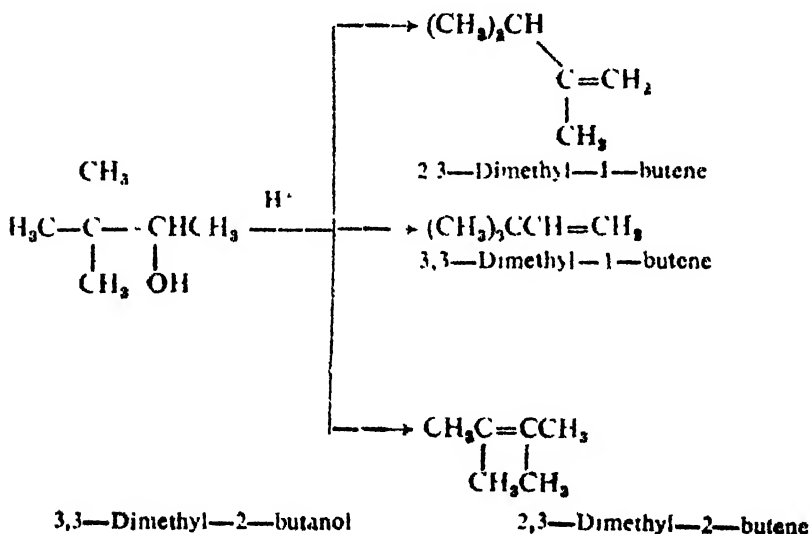
A mixture of the two products is usually obtained.

As has been noticed, both E1 and S_N1 reactions have an identical slow step, therefore, a change in the concentration or the nature of the base does not affect the rate. In general, factors that lead to S_N1 reaction would also normally favor E1 as well. Since a rupture of the carbon-halogen bond takes

place in the activation process, the rate among the halides decreases in order $R-I > R-Br > R-Cl > R-F$. Furthermore polar solvents speed up the rate of the reaction by stabilizing the cation. During dehydration of

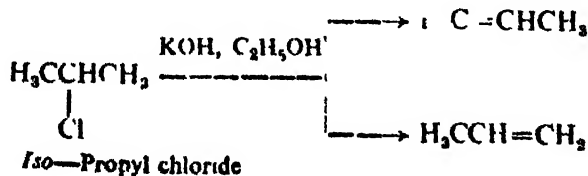


alcohols, rearrangement to a more stable carbocation takes place. This results in the formation of products not predicted on the basis of elimination. This is evident from the dehydration of 3,3-dimethyl-2-butanol in which case 2,3-dimethyl-2-butene and 2,3-dimethyl-1-butene are obtained due to rearrangement. The third product 3,3-dimethyl-1-butene is the normal elimination product.



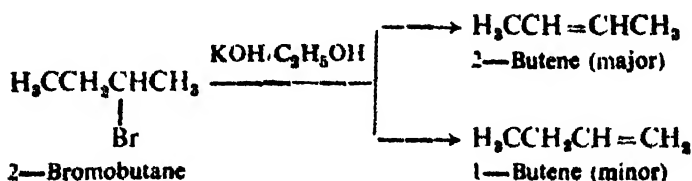
13.7.3 Orientation in Elimination

In a symmetrical organic halide the elimination of HX gives rise to a single alkene, for instance 2-chloropropane forms 1-propene.



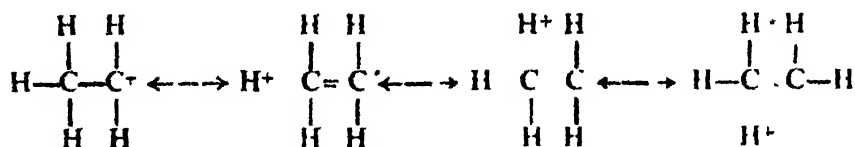
In many cases the elimination may proceed in more than one direction. A

mixture of isomeric alkenes thus results from an unsymmetrical halide as for instance, from 2-bromobutane.

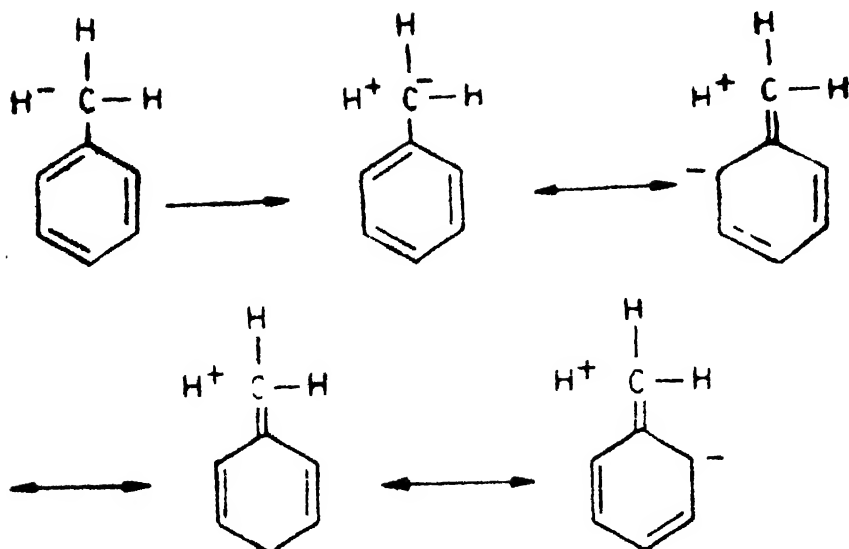


The two alkenes are formed in unequal proportions, the more highly substituted alkene being the major product: Various studies indicate that the elimination can be predicted by the *Saytzeff rule* (Alexander Saytzeff, 1875, University of Kazan, USSR). This rule states that the alkene with the least number of hydrogen atoms attached to the double bond is formed in largest proportion.

The explanation advanced for the formation of the highly substituted alkene is that such an alkene is stabilized by an effect called *hyperconjugation*. This effect arises from the delocalization of σ -electrons of an alkyl group into an adjacent π -bond. To understand this effect let us consider the ethyl carbocation. The following canonical structures can be written for this ion.



In each of these structures the positive charge on the carbon atom has been dispersed after splitting a C-H bond and making a C=C bond. The hydrogen atom carries the positive charge but there is no bond between the hydrogen and the carbon atom. For this reason, resonance of this type is also called *no-bond resonance*. Hyperconjugation is also stabilizing though much less so than resonance. The electron-donating effect of a methyl group in toluene can similarly be explained on the basis of hyperconjugation by drawing the following hyperconjugative structures.



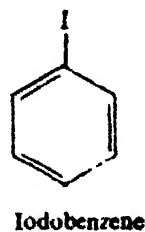
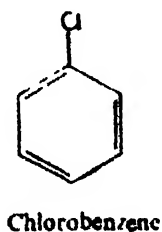
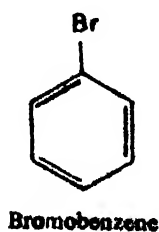
Hyperconjugation besides predicting the stability of alkenes, has also been used in interpreting several other experimental observations.

Section B: ARYL HALIDES

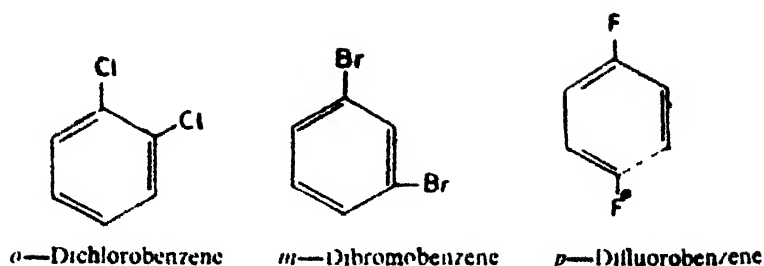
Aryl halides are those compounds in which the halogen atom (F, Cl, Br, I) is attached directly to a benzene ring. The aryl group in such compounds is denoted by the symbol $\text{Ar}-$ to distinguish it from the alkyl group $\text{R}-$. They differ from alkyl halides in many of their properties. The compounds do not occur naturally but are prepared industrially in large quantities.

13.8 NOMENCLATURE OF ARYL HALIDES

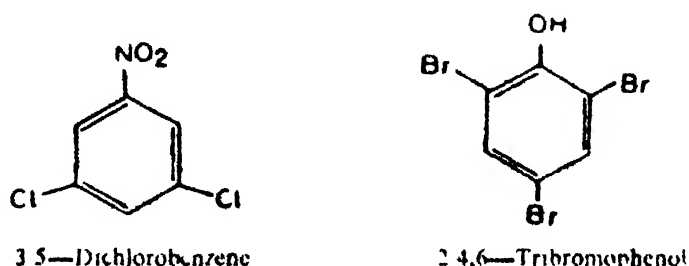
The simple aryl halides are named by using the halo atoms as *prefix* to the word benzene



The three substituted isomers are differentiated by the use of *ortho*, *meta* and *para*.

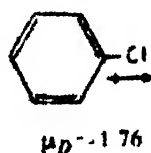


Numbering, however, is needed when more than two halo atoms or other substituents are present on the ring. The halo atoms in the latter case are considered as substituents.



13.9 PHYSICAL PROPERTIES OF ARYL HALIDES

Aryl halides are insoluble in water but soluble in most organic solvents. The boiling points of chlorobenzene and bromobenzene are similar to their open-chain counterparts, i.e., *n*-hexyl chloride and *n*-hexyl bromide respectively. But in the aryl halide series the boiling points increase with the increase in the atomic weight of the halogens. All monosubstituted aryl halides possess a dipole moment because of the more electronegative halogen atom. Chlorobenzene, for instance, has $\mu_D = 1.76$, the value is lower than that of methyl chloride ($\mu_D = 1.94$). The difference is attributed to two factors – first the lone pair on the chlorine atom overlaps the π -orbital



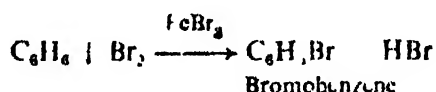
of the benzene ring and secondly because the C–Cl bond in chlorobenzene may be represented as $C_{sp^2}-Cl_p$, while in methyl chloride as $C_{sp^3}-Cl_p$. Therefore, the higher *s* character of the benzene carbon atom makes it electron-withdrawing which lowers the dipole moment. The dipole moment of multisubstituted benzene derivatives are close to the vector sum of the

constituent dipoles. Thus, for *p*-dichlorobenzene, the net dipole moment is zero. The two component C—Cl dipoles oppose and cancel each other.

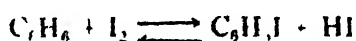
13.10 PREPARATION OF ARYL HALIDES

The following typical methods are employed for the preparation of aryl halides.

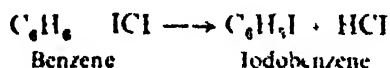
1. *Halogenation* Chlorination or bromination of benzene can be effected in the presence of a halogen carrier or a catalyst, i.e., a Lewis acid. The function of the catalyst is to make the halogen a better electrophile.



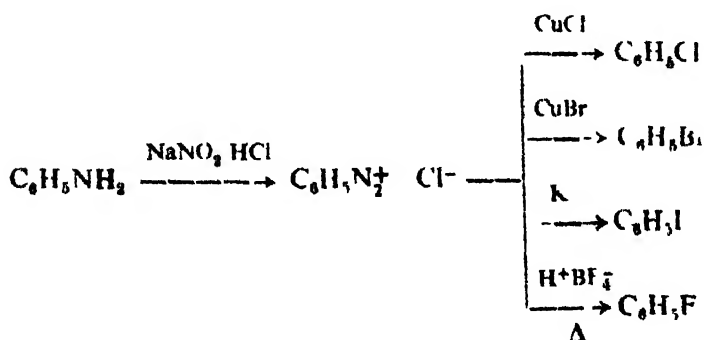
Only bromination and chlorination is possible with aromatic compounds. In case of iodination, the reverse reaction is much faster than iodine substitution.



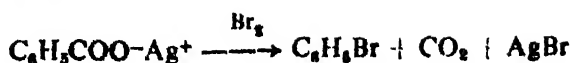
One device used to prevent the reversal of the iodination reaction is the use of iodine chloride.



2. *From Diazonium Salts* This is the most general method used to prepare all types of aryl halides. An aromatic amine is first diazotized which then can be reacted with a metal halide to obtain an aryl halide.



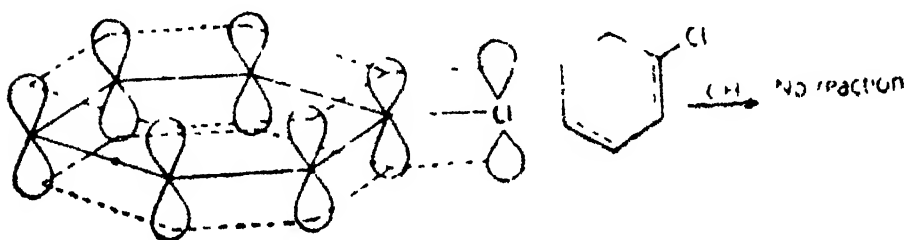
3. *Hunsdiecker Reaction*: Treatment of silver salt of benzoic acid with bromine yields bromobenzene.



13.11 REACTIONS OF ARYL HALIDES

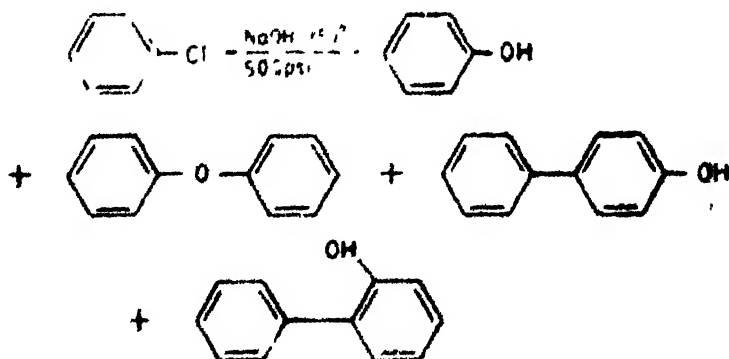
Aryl halides behave different chemically than alkyl halides in many respects.

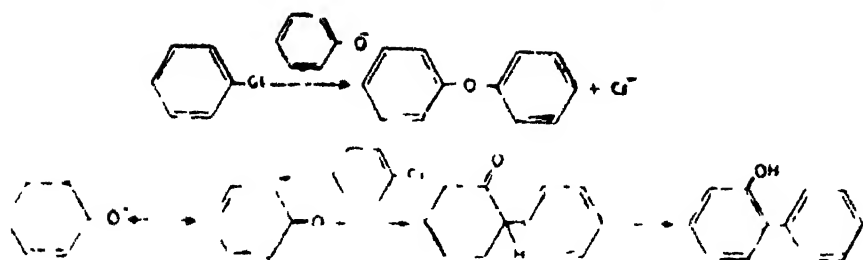
1. *Nucleophilic Displacement*: It was discussed in section A that the alkyl halides undergo nucleophilic displacement with typical nucleophiles with great ease. The aryl halides, on the other hand, react with great difficulty. Chlorobenzene, like vinyl chloride under normal conditions does not hydrolyze to give phenol. The reason for this unreactivity is that the π -orbital of the benzene ring overlaps with the p -orbitals of the chlorine atom to form a delocalized cloud of π -electrons with the result that the



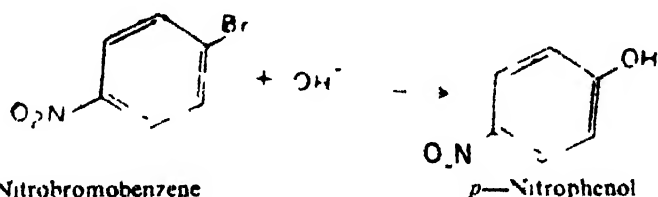
carbon halogen bond attains a partial double bond character. This makes the σ -bond stronger and it becomes difficult to displace the halogen atom. Hydrolysis may be achieved under rather drastic conditions, but several by-products are also formed in the reaction as shown below:

These products are formed by the action of phenoxide ion on chlorobenzene





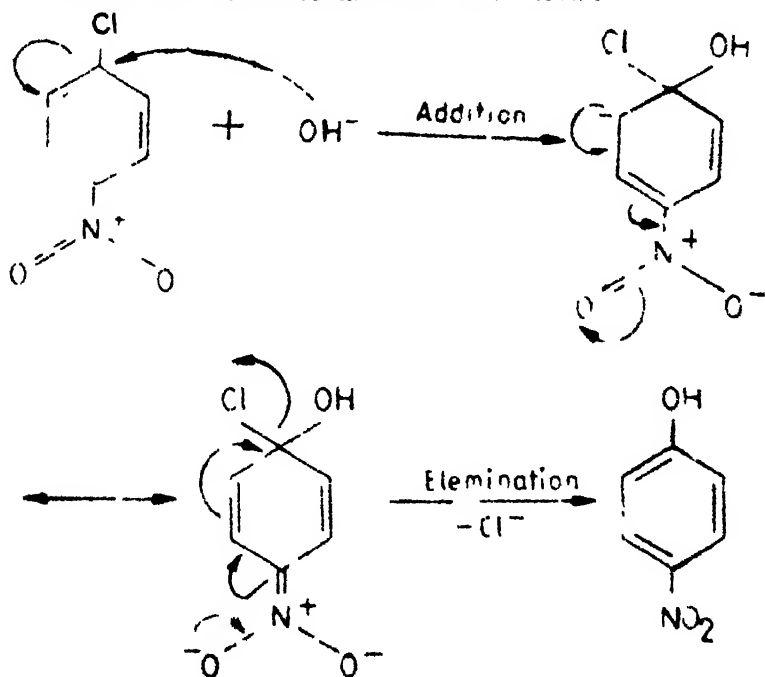
The displacement of the halogen atom occurs rapidly if the ring is activated, i.e., electron-withdrawing groups are present on the ring at the *ortho* or *para* positions. Thus *p*-nitrobromobenzene reacts readily with a base to form *p*-nitrophenol. Presence of a nitro group has an activating effect.



The chlorine atom in 2,4,6-trinitrochlorobenzene is displaced with a dilute base even at $35^\circ C$.

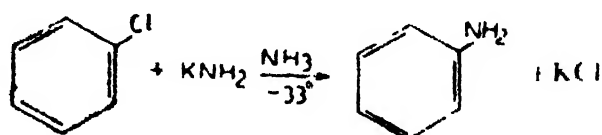
Mechanism

An addition-elimination mechanism is involved in these substrates. A hydroxide ion first adds at the carbon atom bearing the halogen atom. This forms a resonance stabilized carbanion as shown below :

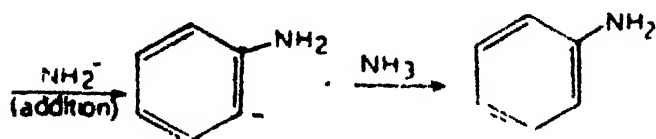
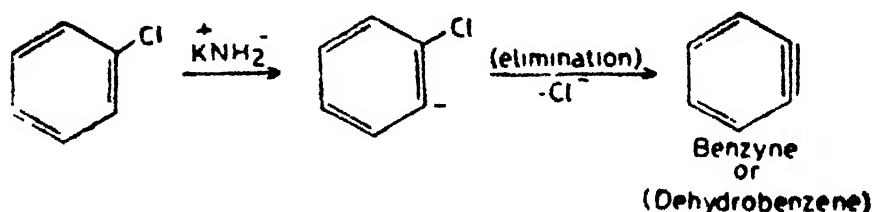


In the next step electron shift takes place and the chloride ion is eliminated. It is apparent that a nitro group at the *meta* position will not be capable of providing such an activating effect.

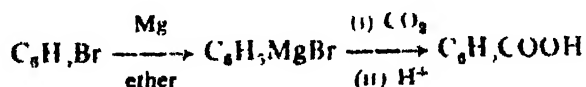
Chloro- or bromo-benzene can react with a strong base like potassium amide in liq. ammonia to give aniline.



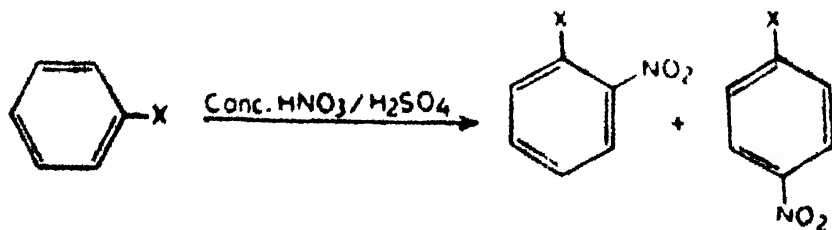
This reaction occurs through an elimination-addition mechanism that involves the formation of an intermediate called *benzyne*, and consists of the following steps:



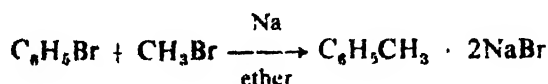
2. Aryl halides form Grignard reagents with magnesium in dry ether. The reagent on treatment with solid carbon dioxide and subsequent acid hydrolysis forms benzoic acid



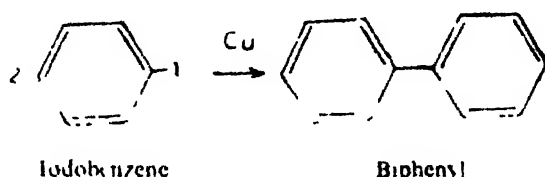
3. *Electrophilic Substitution*: The aryl halides undergo nitration, sulfonation, halogenation and Friedel-Crafts reaction. The halo atom is *ortho* and *para* directing.



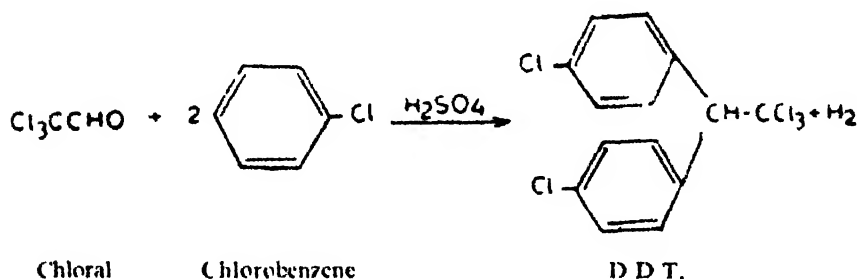
4. **Wurtz-Fittig Reaction:** Alkylaryl hydrocarbons can be prepared by heating an aliphatic halide with an aryl halide in the presence of sodium and dry ether, several by-products, such as ethane and biphenyl are also formed.



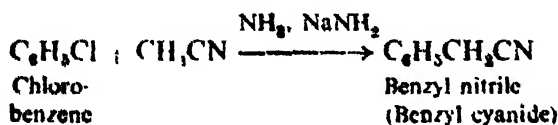
5. **Ullmann Reaction:** In this reaction a biphenyl is obtained by heating iodobenzene in the presence of copper.



6. **Formation of D. D. T:** The most familiar insecticide, 1,1,1-trichloro-2,2-bis-(*p*-chlorophenyl) ethane is obtained from the reaction of chlorobenzene and trichloroacetaldehyde in the presence of catalytic amount of sulfuric acid.

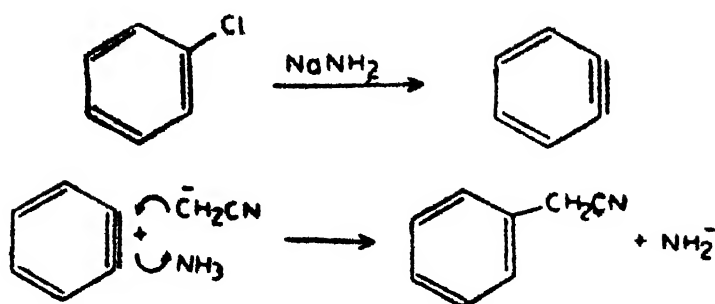


7. Aryl halides react with acetonitrile in the presence of ammonia and sodium amide to form benzyl cyanide.

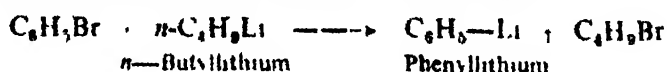


Mechanism

The reaction proceeds through the initial formation of a benzyne. The anion of acetonitrile attacks this intermediate in the manner shown below:



8. *Formation of aryllithium*· Transmetalation of aryl halides with *n*-butyllithium results in the formation of aryllithium



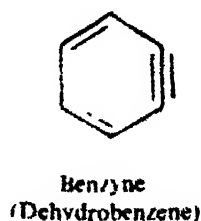
Like phenylmagnesium bromide, phenyllithium on treatment with solid CO_2 and subsequent hydrolysis yields benzoic acid.

13.12 USES OF ARYL HALIDES

Aryl halides are used as starting materials for many organic syntheses. Chlorobenzene is used to manufacture DDT and as a solvent in the laboratory.

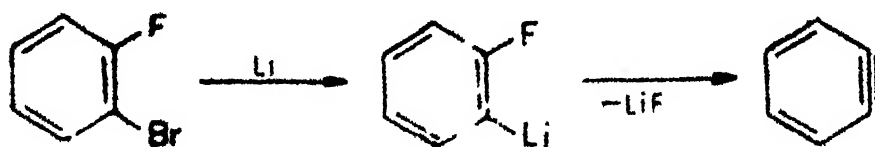
13.13 BENZYNES

If sufficient strain is built into a molecule it can become so unstable that it attains the character of a reactive intermediate. A benzyne is such an intermediate. It is benzene minus two *ortho* hydrogens and is thus also

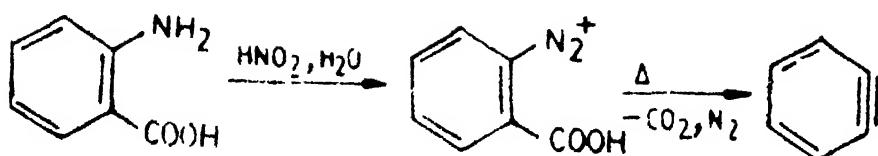


termed as *dehydrobenzene*. The triple bond does not have the same characteristics as in acetylene. This intermediate may be generated by the following methods:

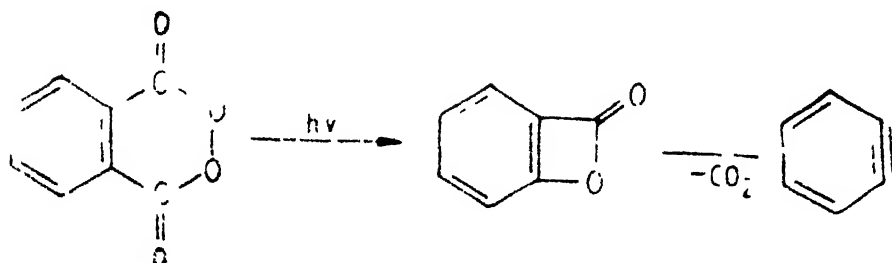
From Bromofluorobenzene



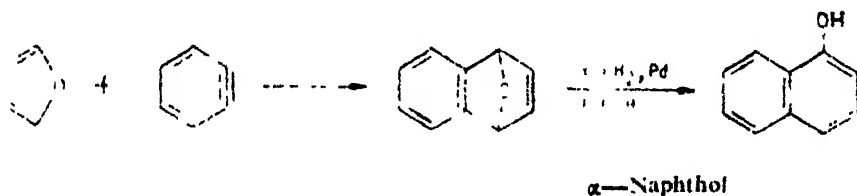
From Anthranilic Acid



From Phthaloyl Peroxide

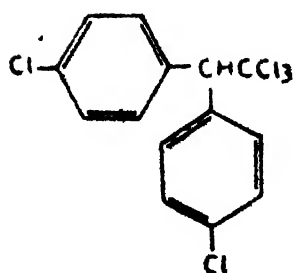


Benzynes undergo many interesting reactions. A benzyne functions as a reactive dienophile in the Diels-Alder reaction. The adducts obtained are valuable synthetic intermediates, as illustrated by the following example.

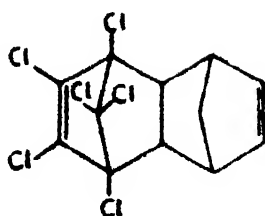


13.14 PESTICIDES

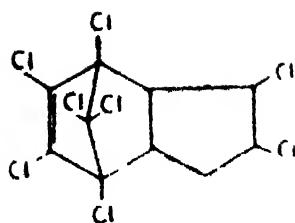
Because of the enormous increase in the world population, the demand for food production has increased. Much success, no doubt, has been achieved in this direction by the use of chemical fertilizers, adapting better farming techniques as well as educating the farmers. In spite of these efforts, a large part of the crops around the world is destroyed by pests. This is a highly undesirable aspect considering that thousands of people go without food daily. In addition to depriving man of food, pests destroy clothing, books and furniture; transmit diseases; and are a source of nuisance to man. The problem of pest control has been a serious problem since prehistoric times. Pests are nowadays being destroyed by spraying chemicals, and *pesticides* are chemical agents that kill and prevent the growth of pests. The term *insecticide* is used to mean the chemicals that kill insects. A list of commonly employed chlorinated hydrocarbons which are used as insecticides is given below:



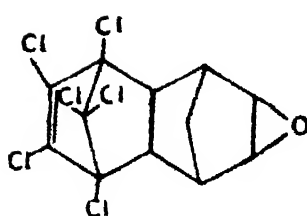
D.D.T.



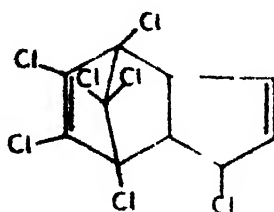
Aldrin



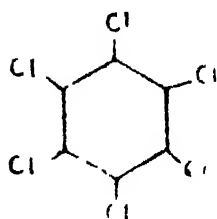
Chloradane



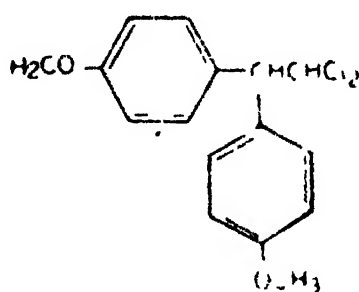
Dieldrin



Heptachlor



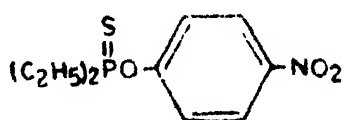
Lindane



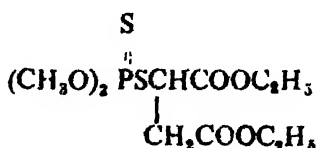
Methoxychlor

DDT was first synthesized in 1874. It is a white powder insoluble in water but soluble in oils. It is used as an insecticide for sugar and fodder crops to kill mosquitoes and other insects. It is decomposed by iron and is not packed in iron containers. DDT is the most widely used insecticide in countries around the world. It, however, has its own ecological problems as it is not biodegradable. This fact seems to have been corroborated by the appearance of DDT in fish and other aquatic animals which are consumed by human beings. Several studies seem to show that DDT interferes with the human reproductive system by disturbing the metabolism of sex hormones. As a result, the use of DDT has been limited in several western countries. In poor nations of the world, however, the benefits appear to be more substantial than the risks involved, DDT is cheap and has a remarkable effectiveness against controlling a number of insects.

Biodegradable insecticides are being used nowadays in place of chlorinated hydrocarbons. Several important ones are listed below:



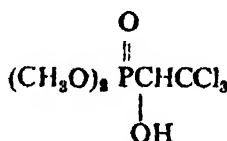
Parathion



Malathion



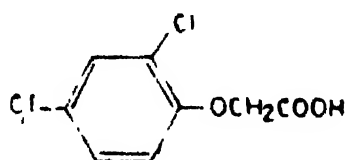
Fenthion



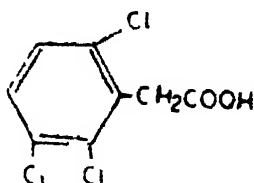
Diox

All of these compounds have similar structures and are characterized by the presence of a phosphorus atom. They are toxic to warm-blooded animals and to insects. They appear to act as powerful inhibitors to *cholinesterase*, an enzyme present in nervous tissue.

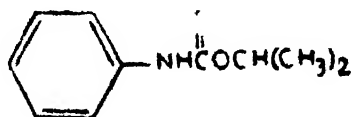
Herbicides: Practically all kinds of plants ranging from trees to microscopic plants may become weeds. These are undesirable plants since they consume water and fertilizers at the expense of crops. Besides their growth causes serious problems in the irrigation of ditches, parks, etc. The weeds are also poisonous to public because of the presence of poison ivy and hay fever plants. Chemicals employed to destroy weeds are known as *herbicides*. The structures of some common herbicides are given below:



2,4-D or 2,4-Dichlorophenoxyacetic acid



Tenac

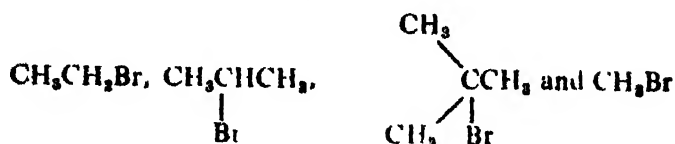


IPC

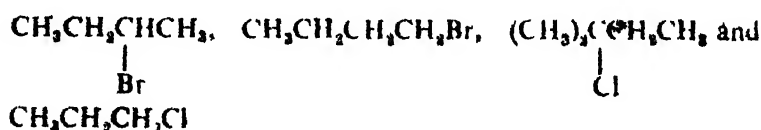
The phenoxyacetic acids are, however, the most commonly employed herbicides. Their function probably includes a breakdown of starches to sugars, deranged cellular growth and reduction in photosynthesis.

QUESTIONS

- 13.1 a. Arrange the following alkyl bromides in order of decreasing reactivity towards iodide ion in dry acetone.

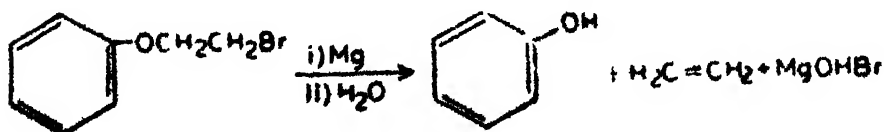


- b. Arrange the following alkyl halides in order of increasing reactivity to $\text{S}_\text{N}2$ displacement.

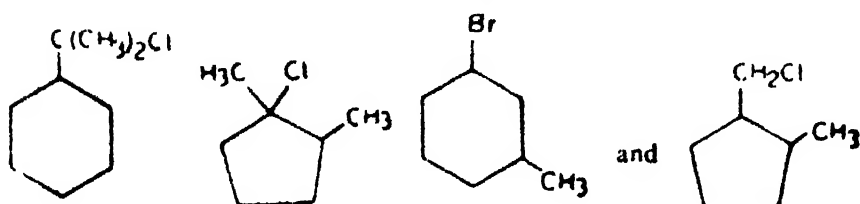


- 13.2 Discuss the various techniques of distinguishing between $\text{S}_\text{N}1$ and $\text{S}_\text{N}2$ reactions
- 13.3 How will you distinguish between the following?
1-Chlorobutane, 1-Chloro-1-butene and 1-Chloro-2-butene
- 13.4 Offer explanation for the following observations:
- Dichlorobenzene has a net dipole moment of zero
 - Vinyl chloride is unreactive in nucleophilic substitution reactions.
 - Chlorobenzene has a lower dipole moment than methyl chloride
 - Alkyl halides, though polar, are insoluble in water
 - The hydroxide ion is incapable of replacing the chloride ion from *m*-nitrochlorobenzene
 - Benzyl bromide is more reactive than cyclohexyl bromomethane with aq. NaOH.
 - $\text{CH}_3\text{CH}_2\text{I}$ is more reactive than $\text{CH}_3\text{CH}_2\text{Cl}$ towards KCN
 - $(\text{CH}_3)_3\underset{\text{H}}{\text{CCH}_2\text{Cl}}$ is very unreactive toward nucleophiles
 - $\text{Cl}-\text{C}_{10}\text{H}_{16}$ is very unreactive toward displacement reactions.
 - DDT is not stored in iron containers.

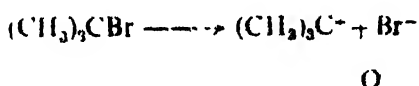
- 13.5 Suggest a mechanism for the following reaction.



- 13.6 Write structural formulas for all the alkyl bromides of the molecular formula $C_7H_{15}Br$. Name each compound.
- 13.7 Indicate the characteristic features of an $E1$ mechanism along with examples.
- 13.8 Assuming only $E2$ elimination write structures for all the possible elimination products from each of the following:



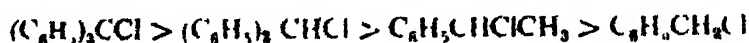
- 13.9 On a potential energy diagram show the course of *meta* and *para* bromination of chlorobenzene.
- 13.10 Assume that acetolysis of *t*-butyl bromide in acetic acid involves the following mechanism.



if addition of sodium acetate to the reaction mixture does not increase the rate appreciably, which step is rate-determining?

- 13.11 An alkyl halide, $C_6H_{11}Cl$, by formation of $Grign^+$ and reagent and subsequent hydrolysis yields 2-methylbutane. Suggest four possible formulas for the original alkyl halide.
- 13.12 A 0.220 g sample of a volatile compound, containing carbon, hydrogen and chlorine only, yielded on combustion no oxygen, 0.195 g CO_2 and 0.0804 g H_2O . A sample of 0.120 g of the compound occupied a volume of 37.24 ml at $105^\circ C$, 768 mm of Hg. Calculate the molecular formula of the compound.
- 13.13 A compound with molecular formula C_6H_{10} does not react with chlorine in the dark, yields a single product, C_6H_9Cl in bright sun light. Write the structure of the original compound.
- 13.14 Compound A of molecular weight ~ 140 contains 25.4% of chlorine and can be hydrolyzed to B, containing no chlorine. Mild oxidation yields C, which reduces Fehling solution. Strong Oxidation of A, B, C gives benzoic acid. Write the structure of A.
- 13.15 A student prepared a pure sample of 1-chloro-2-dimethylaminopropane. After standing for several weeks in a sealed container he opened it and found it was mostly 2-chloro-1-dimethylaminopropane. Resolve the student's dilemma and explain what has happened.

- 13.16 Write the names and structures of some chlorinated hydrocarbons that are useful to crops
- 13.17 Give an example where hydrolysis of an alkyl halide may proceed according to S_N1 mechanism and one example where it may proceed through S_N2 .
- 13.18 Why is S_N2 displacement more difficult with 2-methyl-2-chlorobutane than with 2-methyl-1-chlorobutane?
- 13.19 Prove that hydrolysis of *t*-butyl bromide is S_N1 .
- 13.20 (a) Give the mechanism of the Friedel-Crafts reaction.
(b) What method is employed for the generation of electrophile in each of the following reactions?
(i) Halogenation, (ii) Nitration and (iii) Sulfonation
- 13.21 (a) Give the methods of preparation and the chemical reactions of chlorobenzene
(b) Explain electronically why chlorine in chlorobenzene is less reactive than in benzyl chloride
- 13.22 2-Methyl-2-butene has a resonance energy of 6 kcal/mole compared to 2-butene (4.5 kcal/mole)
- 13.23 When CH_3Br is treated with CN^- the major product is CH_3CN , but some CH_3NC is also formed. Explain
- 13.24 The chlorine atom in *p*-nitro chlorobenzene but not in *m*-nitro chlorobenzene is replaced by $-\text{OH}$ on treatment with aq. NaHCO_3 . Why?
- 13.25 The rate of formation of *t*-butyl ether from the reaction of *t*-butyl bromide with ethanol does not increase if a better nucleophile ethoxide ion is added
- 13.26 The following chlorides undergo solvolysis in the following order. Explain



- 13.27 The following reaction follows S_N2 pathway

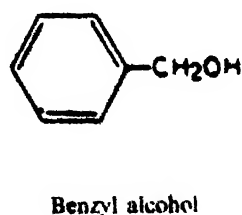
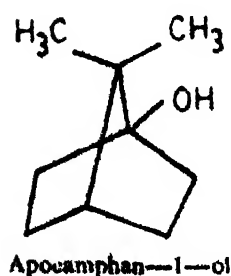
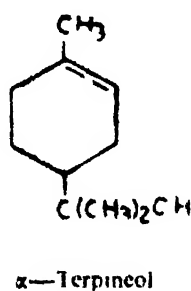
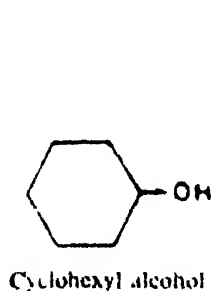
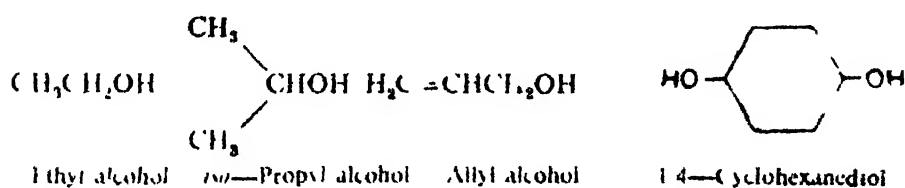


- Write an equation for the expected rate constant
- Draw a potential energy diagram for the reaction
- How would the rate of the reaction change if concentration of sodium azide is doubled?

Alcohols and Phenols

Section A: ALCOHOLS

Alcohols are simple derivatives of aliphatic hydrocarbons, both saturated and unsaturated in which one or more hydrogen atoms are replaced by an $-OH$ group, for example:



Alcohols may be represented by the general formula $C_nH_{2n+1}\cdot OH$ or ROH where R may be an alkyl or an arylalkyl group. Vinyl alcohol is unknown as it isomerizes rapidly to acetaldehyde. Ethyl alcohol or ethanol is by far the most important and is often referred to as alcohol.

The $-OH$ functional group occurs widely in proteins, sugars, starches and many natural and synthetic drugs.

14.1 CLASSIFICATION OF ALCOHOLS

Alcohols are generally classified according to the number of $-OH$ groups present in the molecule. The alcohols containing one $-OH$ group are termed *monohydric*, with two $-OH$ groups as *dihydric* and with three $-OH$ groups as *trihydric*.

Monohydric



Propanol

Dihydric



Ethylene glycol

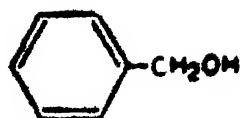
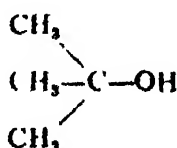
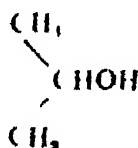
Trihydric



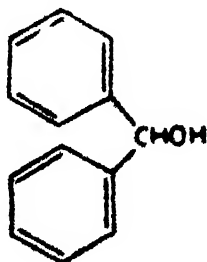
Glycerol

Alcohols containing two or more $-OH$ groups are known as *polyhydric* alcohols.

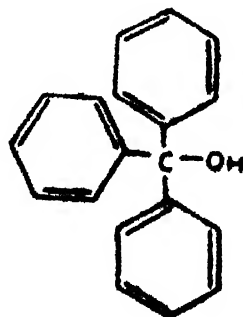
Monohydric alcohols are further subdivided into primary, secondary and tertiary alcohols depending on the number of alkyl groups attached to the carbon atom carrying the hydroxyl group.



Primary



Secondary



Tertiary

14.2 NOMENCLATURE OF ALCOHOLS

Alcohols may be named according to the following three systems:

a. *Trivial Names:* The lower members of the alcohol series are frequently known by their trivial or common names. According to this, the name of an alcohol is derived by combining the name of the alkyl group with the word alcohol. The name is always written as two separate words



Butyl alcohol

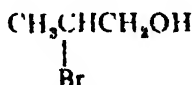


Cyclopentyl alcohol

The position of the substituent present on the carbon chain is indicated by the use of Greek letter α , β , γ , etc., and not by numerals

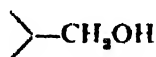


γ -Chloropropyl alcohol

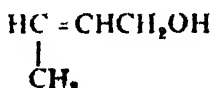


β -Bromopropyl alcohol

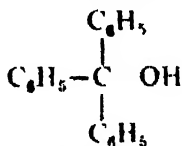
b. *The Carbinol System of Naming:* In this system the first number of the alcohol series, i.e., CH_3OH is called *carbinol*. All other alcohols are considered as substitution products of this compound. The name is written as one word. Ethanol, is thus methylcarbinol and *iso*-propyl alcohol is dimethylcarbinol. Additional examples are



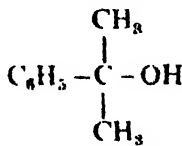
Cyclopropylcarbinol



Methylvinylcarbinol



Triphenylcarbinol

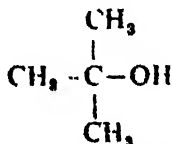


Dimethylphenylcarbinol

The carbinol system is not generally applied to alcohol for which common names are familiar, for example:



Allyl alcohol

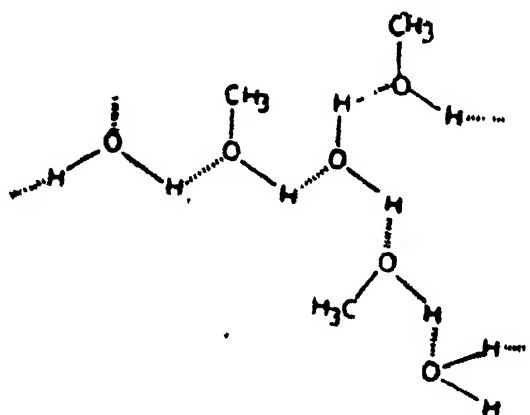


t-Butyl alcohol

c. *IUPAC System of Nomenclature*: This system has been discussed adequately in Chapter 2.

14.3 PHYSICAL PROPERTIES OF ALCOHOLS

Alcohols differ considerably from hydrocarbons in their physical properties. Both alcohols and alkyl halides have much higher boiling points than hydrocarbons containing the same number of carbon atoms, thus *n*-butane boils at -0.5° while *n*-butyl alcohol does so at 117.7° . In the homologous series, the boiling point rises by about 20° for each additional carbon atom (see Table 14.1). Alcohols, in contrast to hydrocarbons are polar. They are soluble in water, which is in marked contrast to hydrocarbons which are non-polar and insoluble. The solubility of alcohols is due to the formation of hydrogen bonds with water. The hydrogen bond formation between water and methanol is shown below:



The methyl alcohol molecules get incorporated into the network of hydrogen bonds in the aqueous solution.

Table 14.1 Physical Constants of Alcohols

Alcohol	m.p. ($^\circ\text{C}$)	b.p. ($^\circ\text{C}$)	Solubility (g 100 g H_2O)
Methyl alcohol	-97	64.5	∞
Ethyl alcohol	-115	78.3	∞
<i>n</i> -Propyl alcohol	-126	97	∞
<i>n</i> -Butyl alcohol	-90	118	7.9
<i>n</i> -Pentyl alcohol	-78.5	138	2.3
<i>n</i> -Hexyl alcohol	-52	156.5	0.5

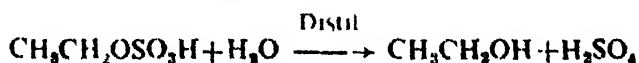
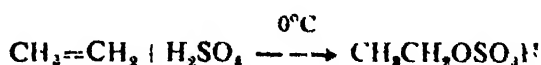
<i>n</i> -Heptyl alcohol	-34	176	0.2
<i>n</i> -Octyl alcohol	-15	195	0.05
<i>iso</i> Propyl alcohol	-86	82.5	∞
<i>iso</i> Butyl alcohol	-108	108	10.0
<i>sec.</i> Butyl alcohol	-114	99.5	
<i>t</i> -Butyl alcohol	-25.5	83	
<i>iso</i> -Pentyl alcohol	-117	132	2
Cyclopentyl alcohol		161.5	
Cyclohexyl alcohol	24	97	
Allyl alcohol	-129	97	
Benzyl alcohol	-15	205	4
α Phenylethyl alcohol		205	
Diphenyl carbinol	-27	22.1	1.6
Triphenyl carbinol	162.5		
Cinnamyl alcohol	33	257.5	

The lower members are highly soluble in water, but the solubility decreases as the carbon chain increases. This change in solubility is accounted for by the fact that a long aliphatic carbon chain with a small —OH group at one end is more like an alkane and is thus less soluble. Branching, on the other hand, greatly increases the solubility in water.

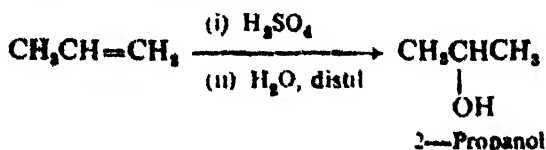
14.4 PREPARATION OF ALCOHOLS

The following general methods may be employed for the preparation of alcohols.

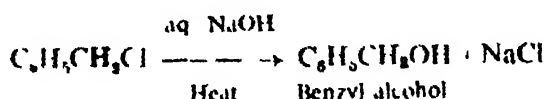
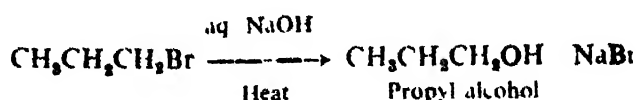
1. *Hydration of alkenes.* This a laboratory preparation for ethanol. Alkenes are obtained by the cracking of petroleum. Alkene is bubbled through conc sulfuric acid at low temperature to form an alkyl hydrogen sulfate. It is subsequently diluted with water and distilled and alcohol is collected.



similarly propene yields 2—propanol.



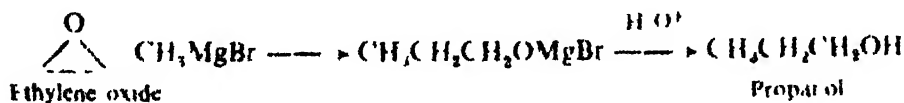
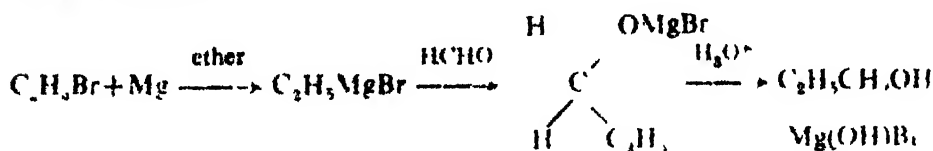
2. *Hydrolysis of Alkyl Halides:* Alkyl halides react with aqueous sodium hydroxide solution to give alcohols. Primary halides react by the S_N2 mechanism.



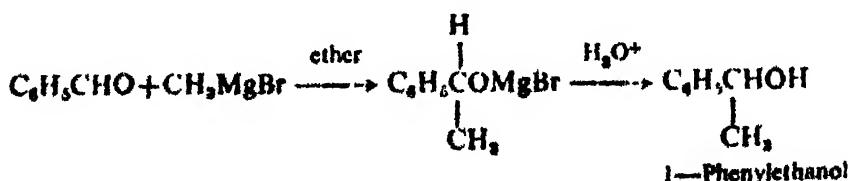
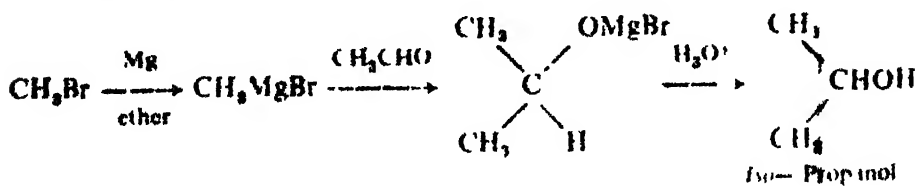
These reactions, however, have limited use because the alkyl halides themselves are obtained by treatment of alcohols with hydrogen halides (HX).

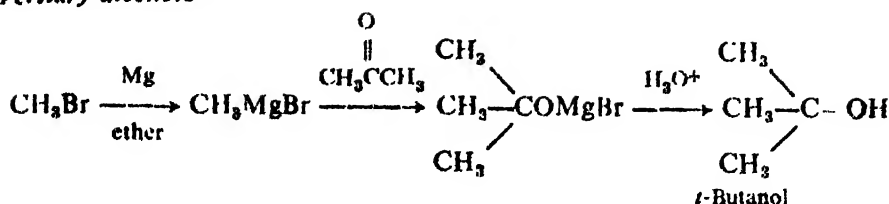
3. *Grignard Synthesis:* This is one of the most important methods for the preparation of alcohols. Primary, secondary as well as tertiary alcohols can be prepared by properly selecting the reagents. A Grignard reagent is first prepared which is then treated with an aldehyde or ketone with subsequent hydrolysis to obtain an alcohol.

Primary alcohols



Secondary alcohols



Tertiary alcohols

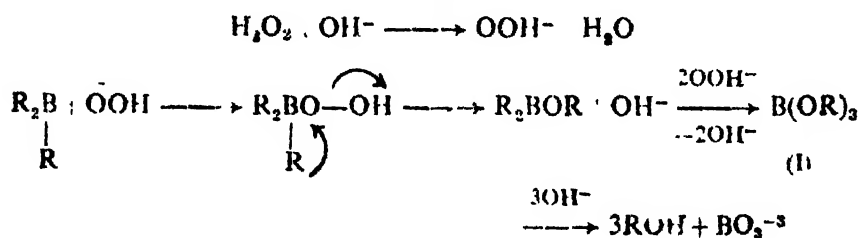
4. **Hydroboration of Alkenes:** The B—H bond of diborane (B_2H_6) rapidly adds on to a C=C bond. The final product is trialkylborane (R_3B),



which need not be separated but can be oxidized with H_2O_2 in a basic medium to yield an alcohol. Hydroboration reactions are *regioselective* and the net result is an *anti*-Markownikoff addition of water.

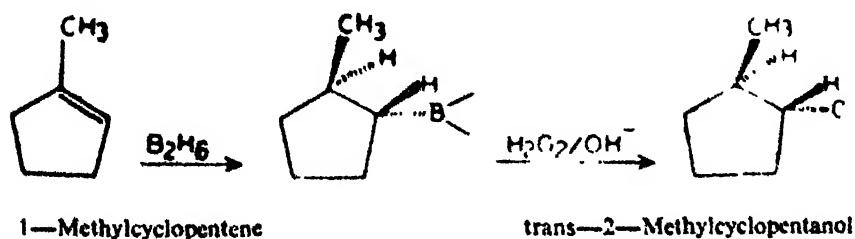
Mechanism

The mechanism involves a nucleophilic attack of the hydroxide anion on alkyl borane, followed by the rearrangement of hydroperoxyboron.

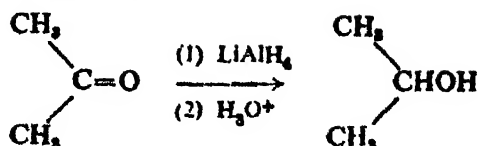


Borate ester (I) is finally hydrolyzed to alcohol.

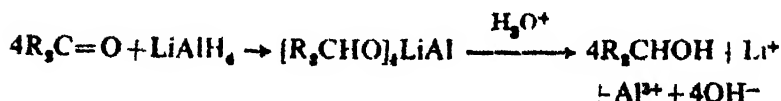
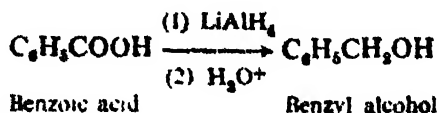
The addition of diborane is controlled by steric effects. The boron atom attacks the less substituted carbon atom *via* a four membered transition state. The addition is stereospecific *cis* and *anti* Markownikoff. It is illustrated by the following example.



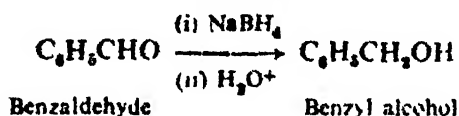
5. **Reduction of Aldehydes and Ketones:** Alcohols may be produced by the reduction of carbonyl compounds by a variety of reagents. Metal hydrides such as LiAlH_4 , NaBH_4 , etc. are often used.



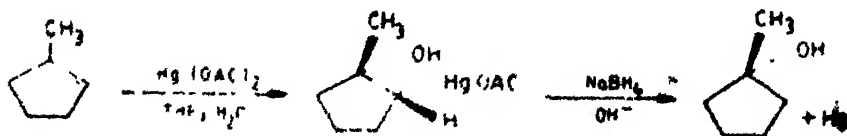
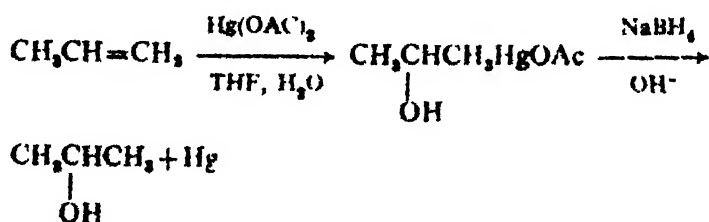
More viable starting materials are carboxylic acids or esters for reduction with LiAlH_4 .



Sodium borohydride may be used under more controlled conditions.



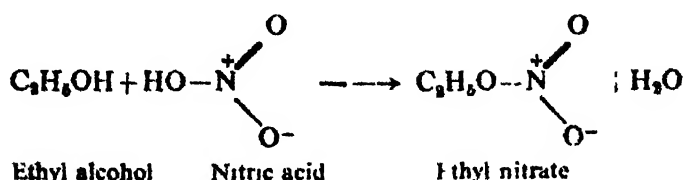
6. *Oxymercuration of alkenes:* A useful procedure for the preparation of alcohols from alkenes is *via* oxymercuration. It is a two step process. An alkene is first reacted with mercuric acetate in a mixture of THF and water. A hydroxyalkyl mercury compound is formed. This is reduced to alcohol with sodium borohydride. The procedure is illustrated by the accompanying examples.



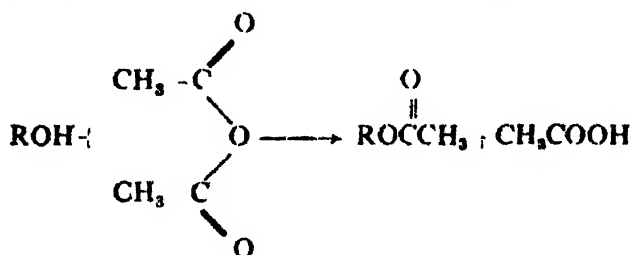
An advantage of this method lies in the fact that skeletal rearrangement, so common in the hydration of alkenes, seldom, take place.

7. *Fermentation (Industrial source):* See Sec. 14.7.2.

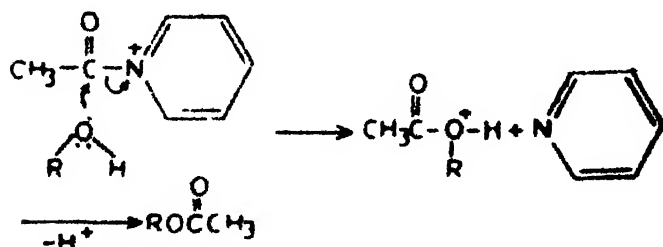
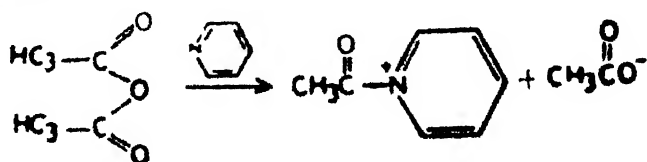
Acyl halides and anhydrides similarly produce esters with alcohols. With nitric acid, nitrates are formed.



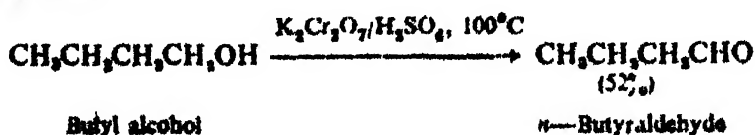
Alcohols are acetylated with acetic anhydride. The reaction may be carried out in the presence of a catalytic amount of pyridine

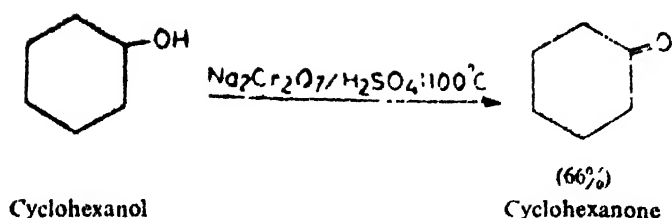


Mechanism

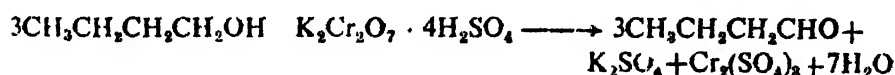


3. Oxidation: Both primary and secondary, but not tertiary alcohols are oxidized to the corresponding carbonyl compounds. This constitutes an important method for the preparation of aldehydes and ketones. The most common oxidizing agents employed are potassium permanganate, KMnO_4 , potassium or sodium dichromate, $\text{K}_2\text{Cr}_2\text{O}_7$ or $\text{Na}_2\text{Cr}_2\text{O}_7$, or chromic acid, H_2CrO_4 . A primary alcohol yields an aldehyde but a secondary alcohol forms a ketone.

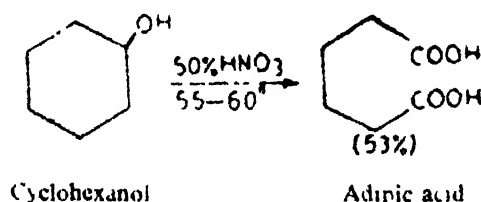




Oxidations by chromic acid (H_2CrO_4) or dichromate ion ($Cr_2O_7^{2-}$) are similar to those of permanganate. These reagents are used under acidic conditions. Sodium and potassium dichromate are commercially available. The complete reaction may be written as follows:

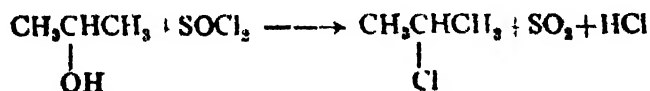


Vigorous oxidation of cyclohexanol in the presence of nitric acid results in the cleavage of the C—C bond and adipic acid is formed.

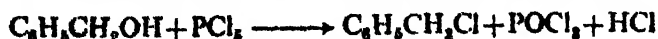


Tertiary alcohols, since they do not contain the grouping $\begin{array}{c} \text{—C—OH} \\ | \\ \text{H} \end{array}$, are not oxidized under these conditions.

4. *Formation of Alkyl Halides:* Reagents like thionyl chloride, $SOCl_2$, phosphorous pentachloride, PCl_5 and phosphorus tribromide, PBr_3 , react with alcohols to form alkyl halides. These reagents are often used to convert alcohols into alkyl halides and are commercially available.

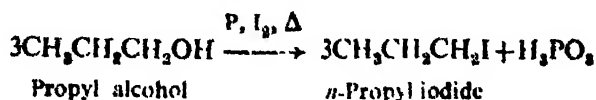


Thionyl chloride often provides alkyl halides of high purity because the other products of the reaction are gaseous. Phosphorus pentachloride reacts in the cold with alcohols, while PCl_3 cannot be obtained.



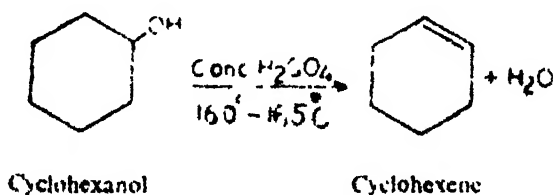
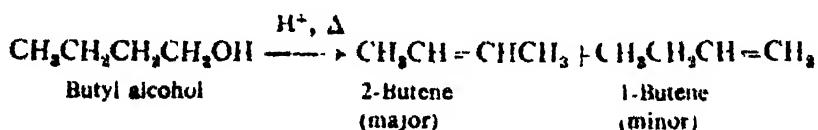
If PBr_3 is not available, red P and Br_2 can be used.

The corresponding phosphorus iodides are not used because they decompose readily, but a combination of red phosphorus and iodine is employed.

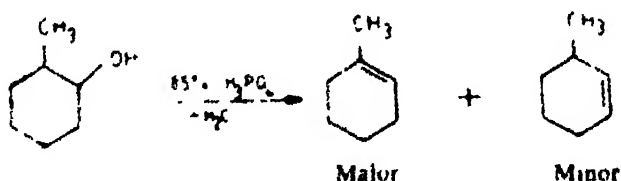


The three hydrohalogen acids HI, HBr and HCl all react with alcohols to form organic halides.

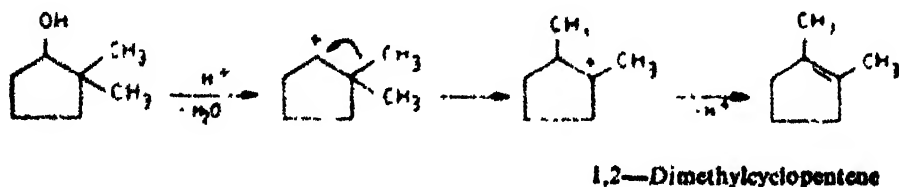
5. **Dehydration:** Alcohols dehydrate on heating (180°) with catalytic amount of sulfuric acid. Below this temperature, i.e., at 140° alcohols form ethers. *n*-Butanol gives a mixture of 2-butene and 1-butene.



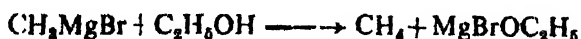
Certain types of alcohols dehydrate to give more than one product. For instance, 2-methylcyclohexanol dehydrates to yield a mixture of 1-methylcyclohexene and 3-methylcyclohexene, the former predominating



Primary and secondary alcohols also undergo skeletal rearrangement during dehydration, as illustrated for 2,2-dimethylcyclopentanol.



6. *Reaction with Grignard Reagents:* Alcohols contain an active hydrogen atom and thus react with Grignard reagents to evolve paraffinic hydrocarbons. Ethanol for instance, liberates methane from methylmagnesium bromide.

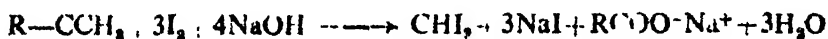
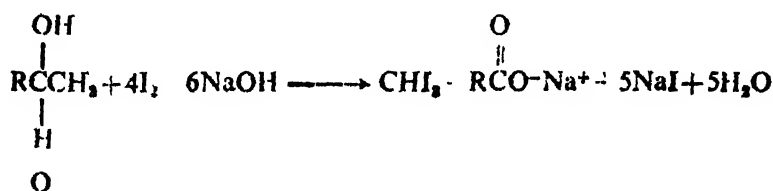


14.6 QUALITATIVE TESTS FOR ALCOHOLS

Alcohols are normally considered neutral compounds. A number of methods that assist in identifying alcohols are available.

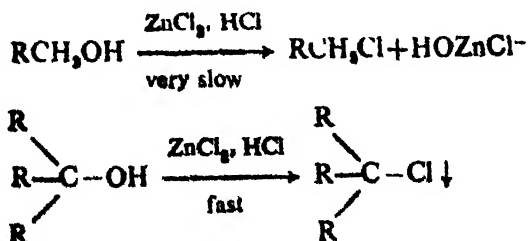
1. *Iodoform Test:* This test is applicable to a particular type of alcohol structure, i.e. alcohols in which the carbon atom bearing the —OH or

$\text{C}=\text{O}$ group is adjacent to a methyl group responds to this test. Thus ethanol but not methanol gives this test. An aqueous solution of alcohol is made alkaline with sodium hydroxide and then iodine solution in potassium iodide is added dropwise and the mixture shaken. In a positive test the brown iodine color disappears and a yellow iodoform is precipitated.



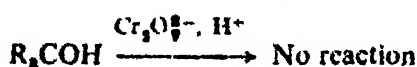
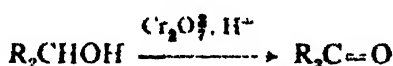
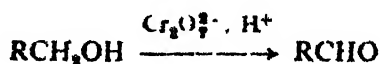
This reaction is very useful because iodoform, which is yellow in color, can be identified by its characteristic odor and melting point. Acetone, acetophenone, ethanol, 2-propanol 2-butanol give this test.

2. *Lucas Test:* This test is applicable to water soluble alcohols. The information obtained by treating an alcohol with conc. hydrochloric acid and anhydrous zinc chloride (*Lucas reagent*) can be used to identify and to classify the alcohols. The test is known as the *Lucas test*. Primary alcohols react very slowly while secondary alcohols show slight turbidity but tertiary alcohols form a halide immediately.



Phenols do not respond to this test even at elevated temperatures.

3. **Oxidation:** Primary and secondary alcohols are distinguished from tertiary alcohols by their oxidation with KMnO_4 or $\text{K}_2\text{Cr}_2\text{O}_7$. The oxidation takes place rapidly and a green or blue color is usually observed with dichromate. Tertiary alcohols fail to show any change within about 2-5 seconds under these conditions. Any reaction taking place in a longer time may be ignored.



14.7 INDUSTRIAL ALCOHOLS

Nowadays more than two dozen alcohols are obtained commercially that are used as starting materials for the preparation of common organic compounds. Simple alcohols are obtained on a large scale for use in industry. We will discuss the preparation of methyl alcohol and ethyl alcohol.

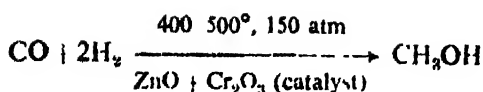
14.7.1 Methyl Alcohol

Methanol is also known as *wood alcohol* because at one time it was obtained on a large scale from the destructive distillation of wood. The main steps in this process are the following:

a. Dried wood is heated in large closed glass retorts in the absence of air at a high temperature (300°C) for several hours.

Dried wood, on heating, yields volatile fractions consisting of gaseous and liquid products; the volatile fraction (coal gas) is used as fuel. The aqueous fraction consists of two layers, the upper layer contains several industrially important chemicals including methanol, the lower dark viscous layer is called *wood tar*. The upper layer is fractionally distilled and the vapors are passed through hot milk of lime and acetic acid is retained as calcium acetate. The resulting vapors, rich in methanol and acetone are condensed. The liquid so obtained is again distilled to separate methanol (b.p. 65°) and acetone (56°C). Methanol of about 90-95% purity is obtained in this manner.

b. **From Water Gas:** Nowadays methanol is produced commercially by a superior method, i.e., from water gas ($\text{CO} + \text{H}_2\text{O}$) in the presence of a catalyst. Water gas is obtained by passing steam over red hot coke which is mixed with excess of hydrogen and the mixture is heated at $300\text{--}400^\circ$ under pressure in the presence of a catalyst. The resulting alcohol is 99% pure.

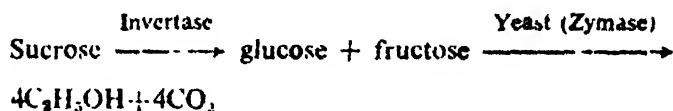


Methanol is poisonous and causes permanent blindness if taken internally. It is sometimes added to ethanol to render the latter unfit for human consumption. This process is called *denaturation* and the alcohol is known as *methyiated spirit*. Methanol is used as a laboratory reagent, as an antifreeze and as a solvent for varnishes and in the preparation of formaldehyde.

14.7.2 Ethyl Alcohol

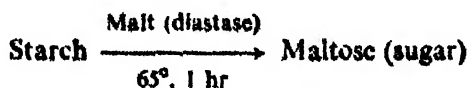
Ethyl alcohol or *grain alcohol* is a very important industrial alcohol and a major section of the chemical industry depends on it as a basic raw material. Two important methods for its manufacture are *fermentation*, i.e. decomposition by living organisms of molasses, sugar or starch (carbohydrates), and synthetically, by the hydration of ethylene obtained during the cracking of petroleum. The actual fermentation reaction is purely chemical but is brought about by specific enzymes secreted by the cell of the organism.

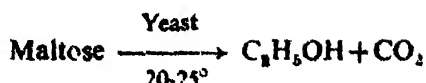
(a) *From Molasses*: For the production of ethyl alcohol good use is made of molasses which is a by-product of sugar industry. It is the mother liquor left during the crystallization of sugar. It is a dark colored viscous liquid which still contains 30% of sucrose and 32% of *invert sugar*, i.e., a mixture of glucose and fructose. Molasses is diluted with water whereby some of the cane sugar dissolves. The diluted solution is fermented with yeast a living plant containing the enzyme yeast, in large tanks. During several days of standing fermentation stops and sugar is converted into ethanol and carbon dioxide.



It is then distilled and the alcohol vapors are condensed and pure alcohol is obtained by careful fractional distillation. The alcohol so obtained is 95% pure (190 proof) b.p 78.3°C the rest being water. The process is known as *rectification* and the alcohol so obtained is referred to as *rectified spirit*. The sale of rectified spirit is controlled legally.

(b) *From Starch (Weizmann Process)*: Ethyl alcohol is obtained by the Weizmann process from starchy materials such as potatoes, rice, maize, grain, barley, etc. This method was developed during World War I to produce acetone a solvent needed in the manufacture of smokeless powder. In addition to acetone (36%), it contains ethyl alcohol (10%). The starchy material is converted by malt into maltose (a sugar) which is then fermented.





Ethyl alcohol is then recovered as in the previous process by distillation.

(c) *Hydration of Ethylene*: We have seen previously that sulfuric acid adds to alkenes which on hydrolysis forms alcohol. The reaction with ethylene is the basis of an important industrial process for the preparation of synthetic alcohol. Ethylene is obtained by partial hydrogenation of acetylene obtained from calcium carbide. This method was developed largely in Germany during the War.



iso Propyl, *sec.* butyl and *t*-butyl alcohols can be prepared similarly.

Ethyl alcohol is used in the dye industry, as a preservative for biological specimens, as a raw material in the preparation of acetaldehyde and acetic acid; as an important laboratory reagent; and as a constituent of motor fuels. It is intoxicating and is used in the beverage industry for making brandy, gin, whisky, rum and other alcoholic beverages. The physiological effect of alcohol is that of a narcotic poison. A *narcotic* is a drug employed to allay pain. Narcotic drugs, when taken in large doses cause coma and convulsions and may prove fatal in very large doses.

Alcohol is miscible with water in all proportions. It is disposed off in the body by oxidation. In the liver it is oxidized to acetaldehyde. Very large concentrations of ethanol are too much for the liver to cope with and may cause damage to the liver.

The redox reaction between ethanol and chromate (VI) is employed in 'breathalyzers'. It contains orange crystals of potassium dichromate (VI) which is reduced to green chromium (III) by ethanol. The color change provides an indication of the level of alcohol vapor in a motorist's breath.

We often talk of energy crisis nowadays. Although coal and oil are being used in large amounts they are strictly limited in quantity. As a result the price of fuels necessary to run machinery is increasing. To alleviate the energy problem Alexander Graham Bell, back in 1917 suggested a solution—burn alcohol. This idea is attracting a great deal of attention. Alcohol can be obtained from very cheap sources and vegetable wastes, for instance, from saw-dust, waste products of farms, vegetable matter, capable of fermentation and even the garbage from the cities.

14.3 ABSOLUTE ALCOHOL

Ethyl alcohol is obtained either industrially or synthetically as a mixture of ethyl alcohol (95%) and water (5%), i.e., an azeotropic mixture. An *azeotropic mixture* may be described as a mixture of liquids of a certain definite composition that distills at a constant temperature without change in

composition. Water can be removed from this mixture to obtain 100% alcohol, referred to as *absolute alcohol*. This is accomplished by distilling ethanol after adding an appropriate amount of benzene. In doing this the first fraction distilling over is a tertiary azeotrope consisting of alcohol, benzene and water. This removes all the water. The alcohol left behind is in an anhydrous state and is distilled (b.p 78.3) to obtain absolute alcohol.

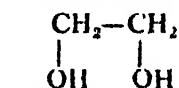
Absolute alcohol is likely to be toxic because of the remaining traces of benzene. Absolute alcohol is 200 proof. A *proof spirit* is a solution of alcohol in water containing one half of its volume of absolute alcohol. Because of the contraction in volume on mixing alcohol with water, 50 ml of absolute alcohol and 53.71 ml of water gives 100 ml of 100 proof spirit. Absolute alcohol is used mainly in lacquers, varnishes and in film industries. *Rubbing alcohol* is usually isopropyl alcohol.

14.9 POWER ALCOHOL

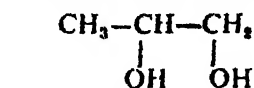
The demand of petroleum is increasing every day. Alternative means of petroleum are needed for energy sources. Industrial alcohol is used for this purpose. It is mixed in the presence of benzene with petroleum and the mixture is employed for the generation of power. This is known as *power alcohol*.

Section B: DIHYDRIC ALCOHOLS

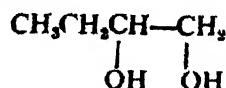
Alcohols containing two hydroxyl groups per molecule are called *dihydric alcohols* or *glycols*. We will be concerned in this section with the compounds containing hydroxyl groups on adjacent carbon atoms. Such compounds are given both common and IUPAC names.



Ethylene glycol

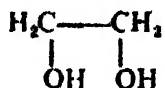


Propylene glycol

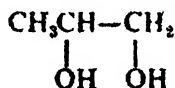


Butylene glycol

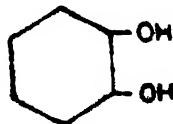
In the IUPAC system, the rules for nomenclature are same as for the monohydric alcohols except that a group suffix *di* is attached to indicate the presence of two hydroxyl groups.



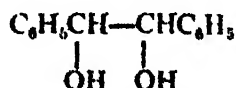
1,2—Ethanediol



1,2—Propanediol

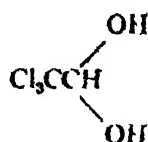


1,2—Cyclohexanediol

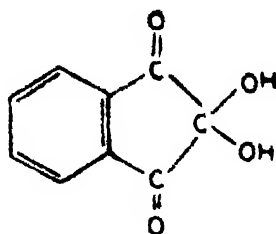


1,2—Diphenyl-1,2—ethanediol

Carbon atoms containing two hydroxyl groups, i.e. *gem* diols are unstable because they readily lose water. However, a few diols, namely chloral hydrate, ninhydrin, etc., are known that are stable



Chloral hydrate



Ninhydrin

14.10 PHYSICAL PROPERTIES OF DIHYDRIC ALCOHOLS

Glycols have high boiling points (Table 14.1) because there are two sites available for hydrogen bonding. The simplest glycol, ethylene glycol, has a b.p. of 197.5°. The lower members are also miscible with water

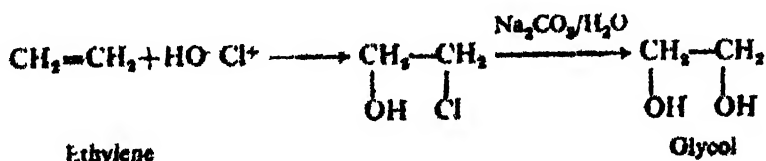
Table 14.1

Glycol	Structure	b.p. (°C)
Ethylene glycol	$\text{HOCH}_2\text{CH}_2\text{OH}$	197.5
Propylene glycol	$\text{CH}_3\text{CHOHCH}_2\text{OH}$	189
Glycoldimethyl ether	$\text{HOCH}_2\text{CH}_2\text{OCH}_3$	124.6
Glycoldimethyl ether	$\text{CH}_3\text{OCH}_2\text{CH}_2\text{OH}$	85.5
Diethylene glycol	$\text{HOCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OH}$	156
Carbitol	$\text{C}_4\text{H}_9\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OH}$	198

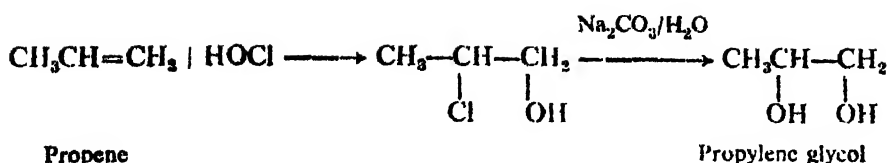
14.11 PREPARATION OF DIHYDRIC ALCOHOLS

Glycols are prepared by reactions that are modifications of the general methods discussed for the preparation of monohydric alcohols.

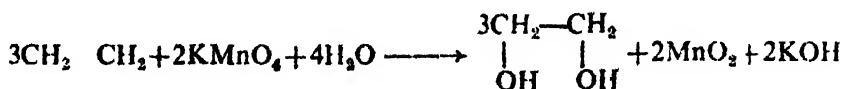
1. *From Ethylene* Addition of hypochlorous acid ($\text{Cl}_2 + \text{H}_2\text{O}$) to ethylene and subsequent hydrolysis of the adduct introduces two hydroxyl groups.



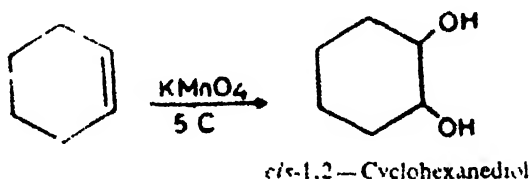
Propylene glycol can be prepared similarly from propene.



2. *Hydroxylation of Alkenes*: Glycols may be obtained by hydroxylation of the double bond of an alkene with KMnO_4 or OsO_4 (Osmium tetroxide)

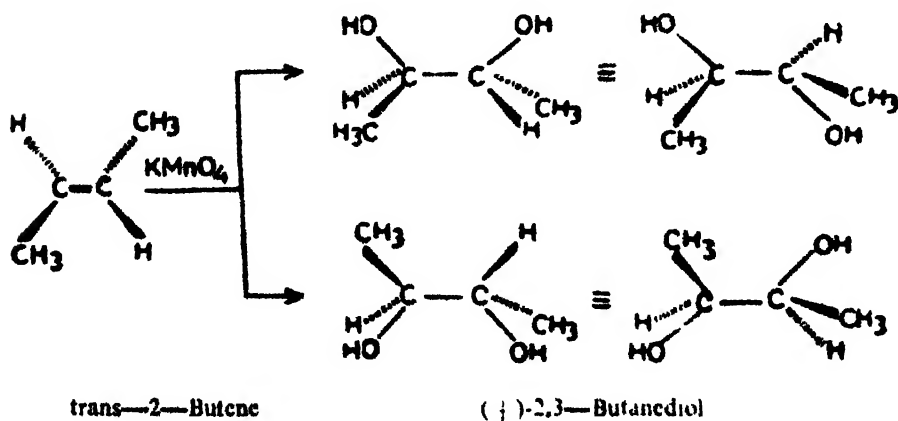


The disappearance of the purple color of aqueous permanganate solution on the addition of an alkene is known as *Bayer's test*.



Mechanism

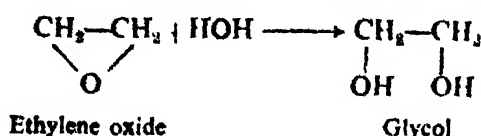
The reaction is stereospecific *cis* addition, i.e., a *cis* olefin produces a *cis* diol, while a *trans*-diol is formed from a *trans* olefin. Hydroxylation of *trans*-2-butene leads to the formation of enantiomeric 2,3—butanediol.



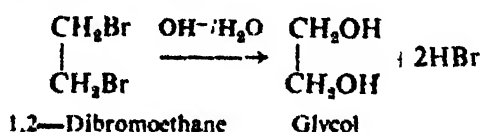
Hydroxylation of the *cis* isomer results in the formation of *meso*-2,3-butane-diol.

3. *From Epoxides*: Ethylene oxide or epoxide is a strained ring and can be converted into many useful products by treatment with different reagents. The carbon-oxygen bond is broken very easily compared to such a linkage in an open-chain compound. This is attributed to the presence of strain due

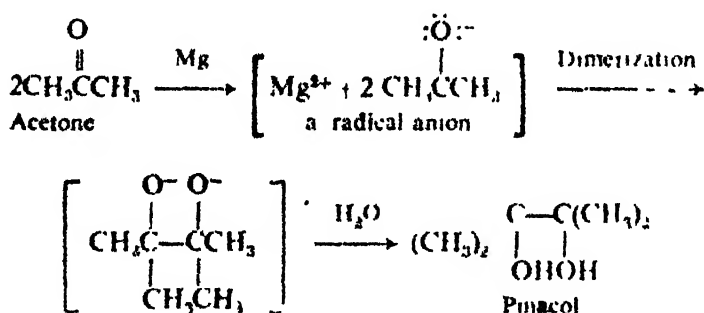
to angle distortion. One of the C—O linkages breaks and positive part of the addendum becomes attached to the electronegative oxygen atom.



4. Hydrolysis of Vicinal Halides: Heating a vicinal halides in the presence of a base also yields a diol.



5. Bimolecular Reduction of Carbonyl Compounds: Symmetrical 1,2-diols may be prepared by the bimolecular reduction of aldehydes and ketones. The reducing agent is generally an electropositive metal such as magnesium.

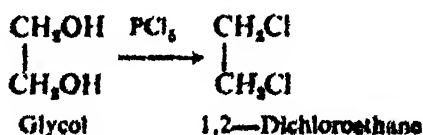


A radical anion is first formed by the transfer of electrons from the metal to the ketone. This is followed by the dimerization of the radical anion to produce the dianion of a 1,2-diol which hydrolyses to the diol. The diol produced from acetone has the trivial name *pinacol*.

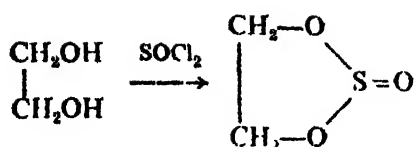
14.12 REACTIONS OF DIHYDRIC ALCOHOLS

Glycols display the following chemical reactions.

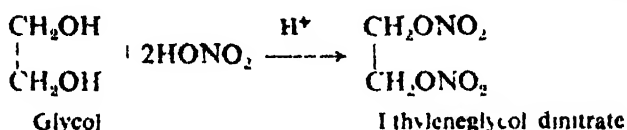
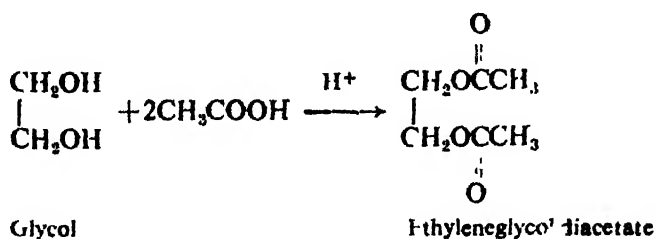
1. Formation of Vicinal Halides: In a manner similar to monohydric alcohols, glycols react with phosphorus halides to form 1,2-dihalides,



With SOCl_2 , glycol forms a cyclic sulfite.

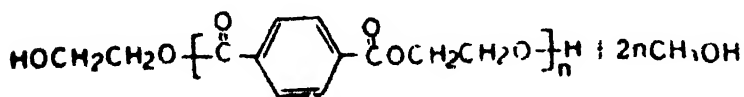
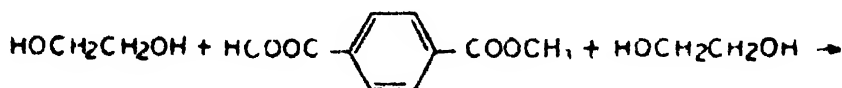


2. **Esterification:** Glycols need two molecules of acids and a catalytic amount of sulfuric acid to form esters.



3. **Polyester Formation:** A dicarboxylic acid when it reacts with a dihydric alcohol, an ester linkage is formed at each end of the molecule.

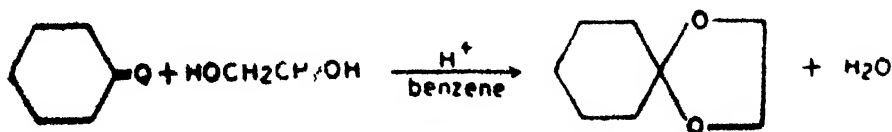
By further reaction many ester linkages may be linked together building up a large molecule. Dacron (known as *Terylene* in U.K.), a synthetic fibre, is such a polyester and is prepared from ethylene glycol and dimethyl terephthalate. The acid is not used because it is difficult to purify.



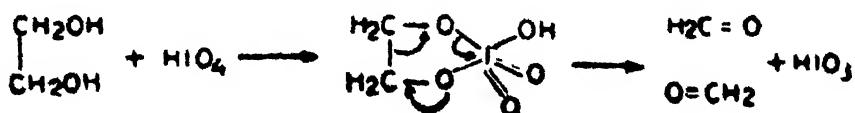
Polyethylene terephthalate

This polyester absorbs little moisture, has a high crease resistant property and can also be converted to a thin fibre (Mylar) of high strength.

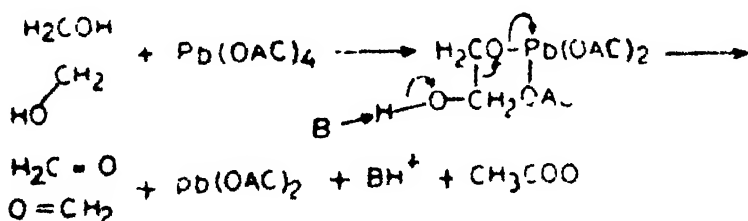
4. **Acetal and Ketal Formation:** Aldehydes and ketones form ring compounds with glycols.



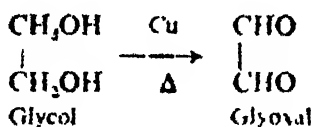
5. Oxidation: Periodic acid brings about a unique reaction of *vicinal* diols. The carbon-carbon bond carrying the hydroxyl groups is broken to yield two molecules of carbonyl compounds. This is known as the oxidative cleavage of diols. The reaction proceeds through the formation of a cyclic ester of periodic acid.



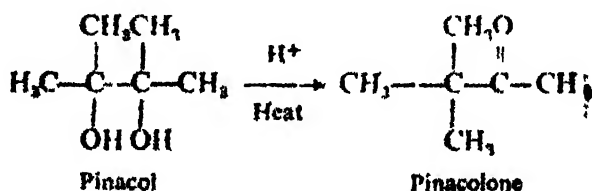
An identical carbon-carbon bond cleavage is also brought about by lead tetraacetate



Glycols are also oxidized to dicarbonyl compounds easily by ordinary methods of oxidation.

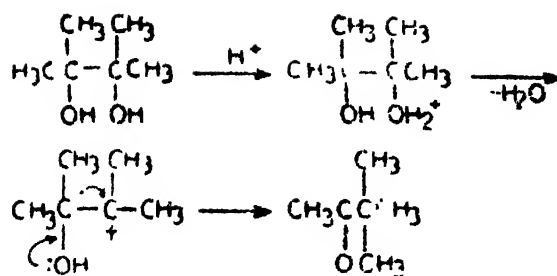


6. Pinacol-Pinacolone Rearrangement: Pinacol as well as other 1,2-diols, on reaction with an acid undergo a rearrangement of an alkyl group to yield pinacolone, i.e. methyl *t*-butyl ketone.



Mechanism

The mechanism of the reaction involves the protonation of one hydroxyl group as the first step. This loses a water molecule to give a tertiary carbocation. Then a 1,2-shift of a methyl group takes place to form the ketone

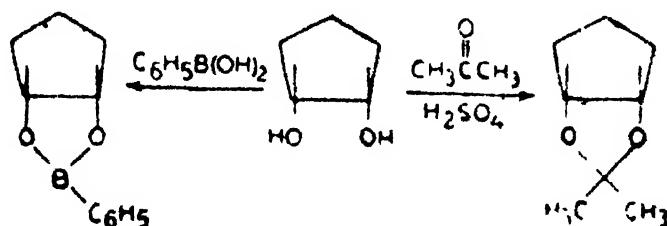


14.13 USES OF ETHYLENE GLYCOL

Ethylene glycol is used as a raw material for making polyester, as an anti-freeze for automobiles, as a cooling agent and a laboratory solvent

14.14 TESTS FOR *cis*— and *trans*—DIOLS

A distinction between *cis*— and *trans*—diols may be made by reacting with acetone or phenylboronic acid. A *cis* diol readily forms a cyclic derivative with these reagents whereas the *trans* form does not.



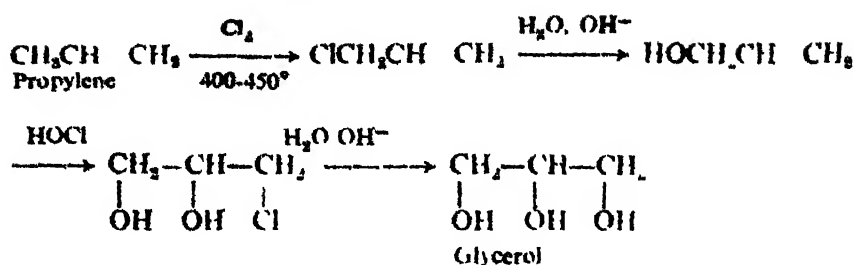
cis—Glycols can undergo cleavage with lead tetraacetate at a much faster rate than the corresponding *trans* isomers

Section C: TRIHYDRIC ALCOHOLS

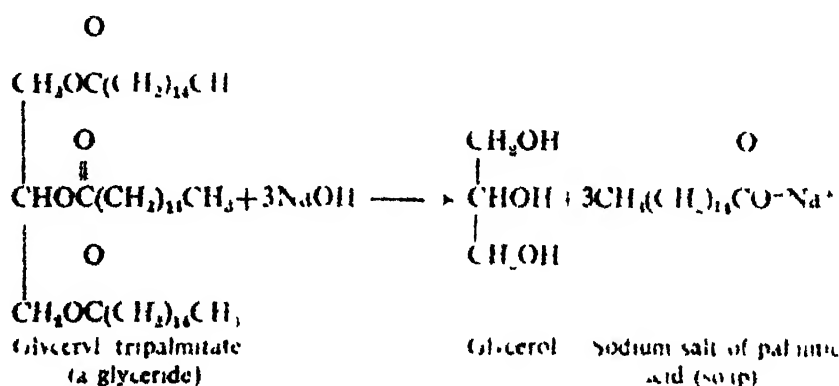
Trihydric alcohols contain three hydroxyl groups on adjacent carbon atoms. They possess the general formula $\text{C}_n\text{H}_{2n+1}(\text{OH})_3$. The most important member of this series is 1,2,3-propanetriol also popularly known as glycerol or glycerine.

14.15 PREPARATION OF TRIHYDRIC ALCOHOLS

1. *From Propylene:* Propylene is chlorinated at a high temperature and the product so obtained is hydrolysed to allyl alcohol. This adds on a molecule of hypochlorous acid and hydrolyzed again.



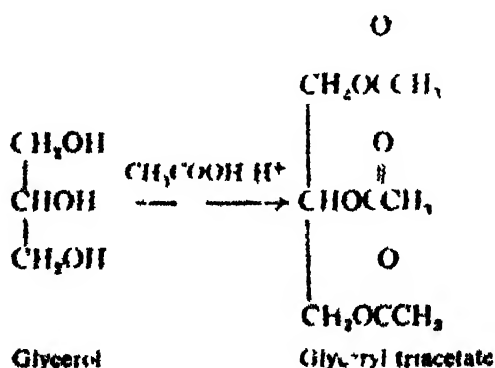
2 *From Soap.* Glycerol is obtained as a by-product in the manufacture of soap. Oils and fats are esters of long chain fatty acids. Hydrolysis with sodium hydroxide yields glycerol and soap.



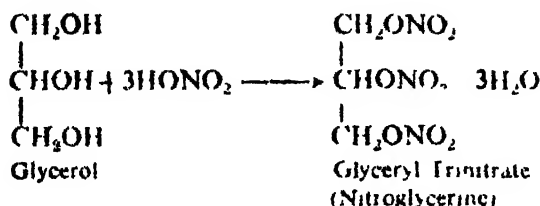
Such esters of glycerol with long chain fatty acids are also known as glycerides. The fatty acids are extracted from animal and vegetable fatty tissues.

14.16 REACTIONS OF TRIHYDRIC ALCOHOLS

1 *Esterification:* Glycerol is esterified with a carboxylic acid in the presence of a mineral acid as catalyst.



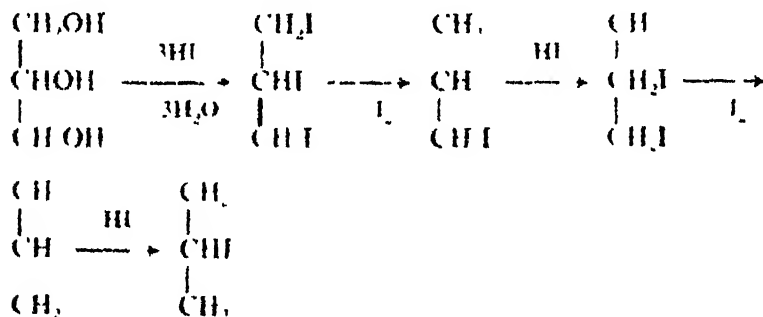
With nitric acid glycerol forms glyceryl trinitrate



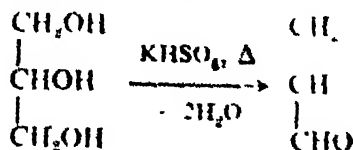
During the period 1866–1875, Alfred Nobel, a Swede made basic discoveries of the application of nitroglycerine as explosive. He made a large fortune from this and he established the famous Nobel prize in science and arts.

Nitroglycerine is detonated by shock: When it is absorbed on Kieselguhr (a type of clay) it is called *dynamite*. It is less sensitive to shock and can be handled safely. Presently only a small amount of nitroglycerine is used as dynamite.

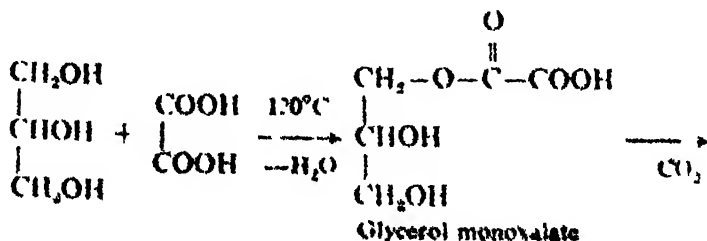
2. *Reaction with HI*: Glycerol on reaction with hydriodic acid leads to 2-iodopropane according to the following sequence of reactions

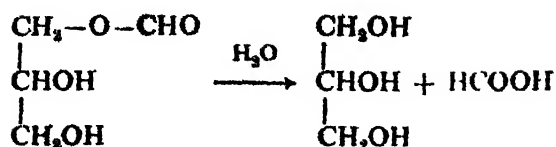


3. *Reaction with Potassium Hydrogen Sulfate*: Glycerol on heating with acidic potassium hydrogen sulfate loses two molecules of water to form acrolein, a pungent smelling compound



4. *Reaction with Oxalic Acid*: A mixture of glycerol and oxalic acid on heating yields formic acid.





Glycerol monoformate

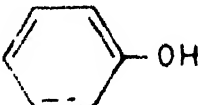
14.17 USES OF GLYCEROL

Glycerol is used for the manufacture of high class toilet soaps and cosmetics; in the preparation of nitroglycerine used in making explosives; and in the resin industry. It is also used in shoe polish and stamp colors. It is a component of several pharmaceutical products and is employed in making dyes and for the preparation of quinoline.

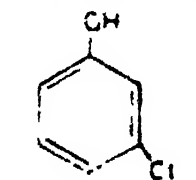
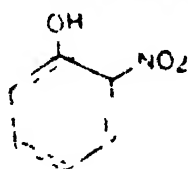
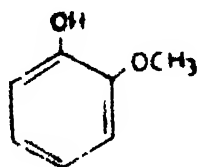
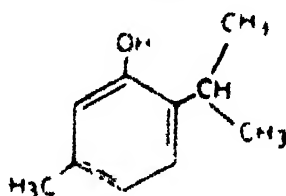
Section D : PHENOLS

Phenols are derivatives of aromatic hydrocarbons in which a ring hydrogen atom is replaced by -OH group. They possess the general formula $\text{Ar}-\text{OH}$ where Ar is a phenyl or substituted phenyl group. Phenols differ from alcohols both in their physical and chemical properties. Phenols give characteristic colors with FeCl_3 solution while aliphatic alcohols do not. Phenols are acidic while alcohols are considered neutral. A number of phenols may be obtained from coal tar.

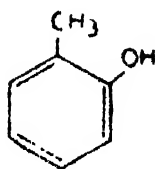
14.18 NOMENCLATURE

The simplest member of the series is called phenol, 

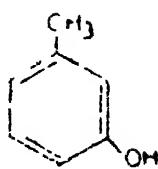
Phenol derivatives are usually named as derivatives of this parent compound. Numerals are used if more than two groups are present on the ring.

*m*-Chlorophenol*o*-Nitrophenol*o*-Methoxyphenol5-Methyl-2-isopropylphenol
(Eugenol)

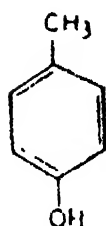
Certain phenols are known by their trivial names.



o-Cresol

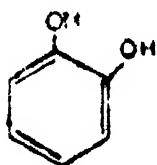


m-Cresol

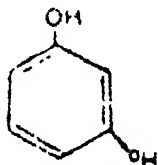


p-Cresol

Compounds having two or more hydroxy groups on the ring also possess common names.



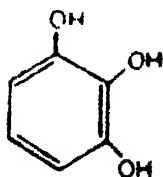
Catechol



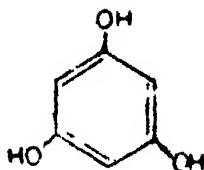
Resorcinol



Hydroquinone
(Quinol)

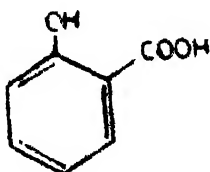


Pyrogallol

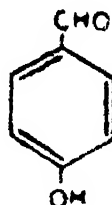


Phloroglucinol

Certain groups like —COOH , —CHO , $\text{—SO}_3\text{H}$, when present on the ring take priority and the hydroxyl group is used as a modifying prefix.



o-Hydroxybenzoic acid
(Salicylic acid)



p-Hydroxybenzaldehyde

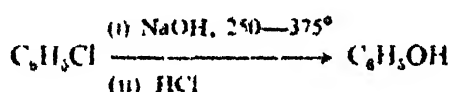
14.19 PHYSICAL PROPERTIES OF PHENOLS

The simplest phenols are liquids or low-melting solids. Phenol itself is a colorless crystalline low melting solid and possesses a medicinal odor and is moderately soluble in water. It must be handled with care as it can cause burns when in contact with skin. Phenols are high boiling compounds because of intermolecular hydrogen-bonding. Since they form hydrogen bonds with water they are soluble in it. Phenols are colorless compounds but turn pink on standing because of atmospheric oxidation.

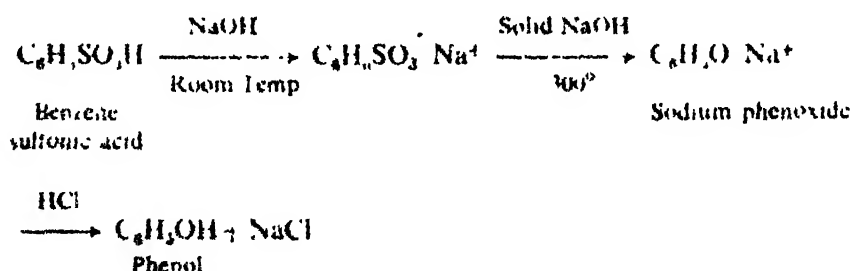
14.20 PREPARATION OF PHENOLS

Phenols are prepared by methods different from those for the preparation of alcohols. The major source of phenols is the petrochemical industry.

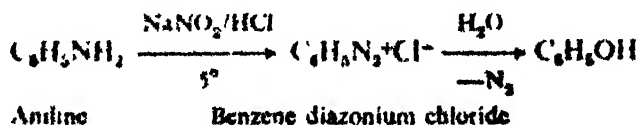
1. **Aryl halides** are quite unreactive towards displacement reactions under ordinary conditions. However, with hot sodium hydroxide and under pressure, hydrolysis takes place. The product sod. phenoxide is converted to phenol by acidification.



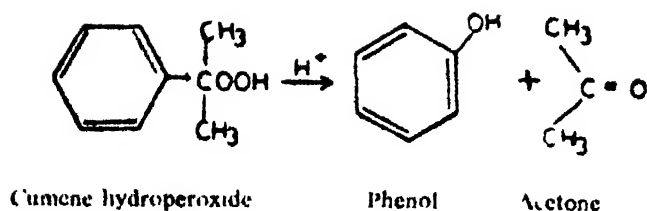
2. **From Sulfonic Acid** An old but useful synthetic method is the fusion of sod. benzenesulfonate with alkali. Sodium phenoxide so obtained is dissolved in water and acidified to obtain phenol.



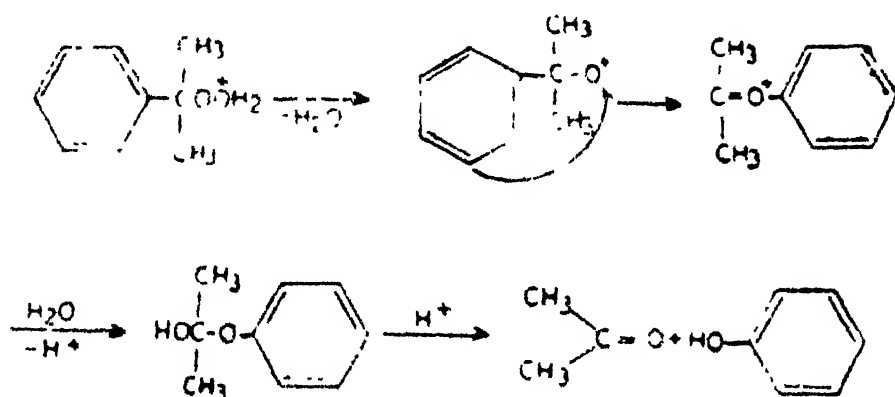
3. **By Hydrolysis of Diazonium Salts:** Aniline or substituted anilines are diazotized with sodium nitrite and hydrochloric acid at low temperature and the resulting diazonium salt forms phenol with water, and nitrogen is evolved.



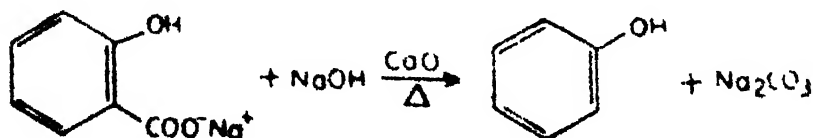
4. **From Cumene Hydroperoxide:** Phenol is produced from cumene hydroperoxide by treatment with sulfuric acid. Cumene hydroperoxide is obtained by autoxidation of cumene, between 95–135°C.

**Mechanism**

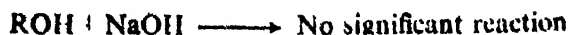
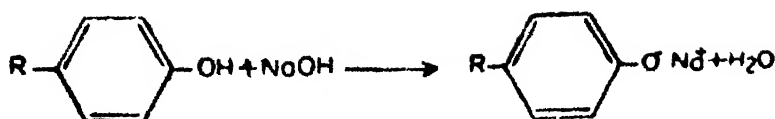
The first step is protonation and then loss of water forms a cationic oxygen atom. Rearrangement of the phenyl group to oxygen takes place. Finally attack by water and loss of H^+ gives phenol



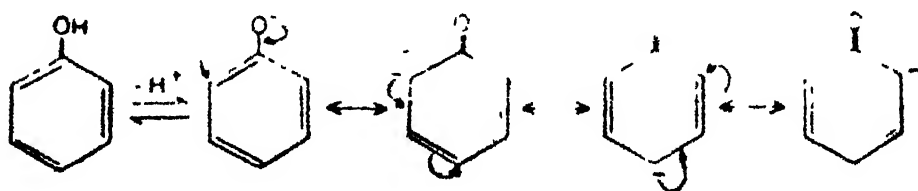
5. Decarboxylation of sod. salicylate with soda lime is also a source of phenol.

**14.21 ACIDITY OF PHENOLS**

As stated earlier phenols and alcohols differ in many of their physical and chemical properties because the aromatic nucleus exerts a strong modifying effect on the properties of the hydroxyl group. One such important property is the acidic nature of phenols, i.e., they are soluble in aqueous sodium hydroxide solution and form sodium phenoxide. Alcohols, on the other hand do not react to any extent with sodium hydroxide. Phenols are acidic, though



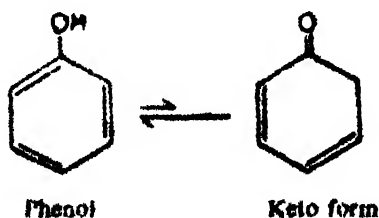
several orders of magnitude less acidic than carboxylic acids, but far more so than alcohols. The acidity of a hydroxyl group varies widely depending on the molecule and its location within the molecule. The correlation of acidity with structure can be best explained if one considers the ionized species for phenol and also ethanol. In anions like alkoxide (OR^-) and hydroxide (OH^-) the full negative charge is localized on the oxygen atom and there is no particular stabilization of the anion. As a consequence these anions are strongly basic and the corresponding acid (ROH) is very weak. On the other hand, in the basic phenoxide ion this is not the case as the negative charge is delocalized over the entire molecule as shown below.



Delocalization of the charge stabilizes the phenoxide ion and thus shifts the ionization equilibrium to favor, formation of the anion, i.e., the phenoxide ion. The resonance theory thus nicely explains this delocalization of the phenoxide ion whereby several contributing structures can be written. The acidity of a phenol can be further augmented by putting electron-withdrawing groups such as $-\text{NO}_2$ on the nucleus. This will have the effect of further delocalizing the negative charge of the ion. Thus *p*-nitrophenol ($K_a = 6.5 \times 10^{-8}$) is 500 times more acidic than phenol ($K_a = 1.3 \times 10^{-10}$) itself.

14.22 REACTIONS OF PHENOLS

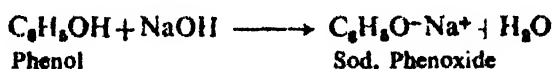
Unlike most enols, phenol is stable in the hydroxy form, because in the



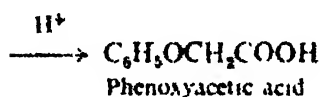
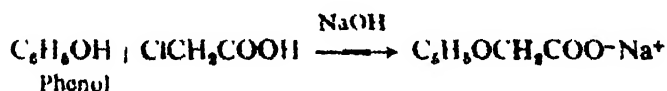
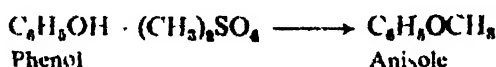
keto form the large stability of the benzene ring is sacrificed.

Phenols do not react with hydrogen halides to form aryl halides because the protonated phenol does not dissociate to form a carbocation which will not be stable. Phenol also does not react with PCl_5 or PBr_5 to give halides. Phenol is not oxidized in the same manner as alcohols.

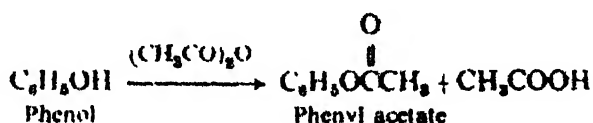
1. **Formation of Salts:** Phenols, being weakly acidic, form salts with strong bases.



2. **Formation of Ethers:** With dimethyl sulfate as the methylating agent phenol forms anisole.

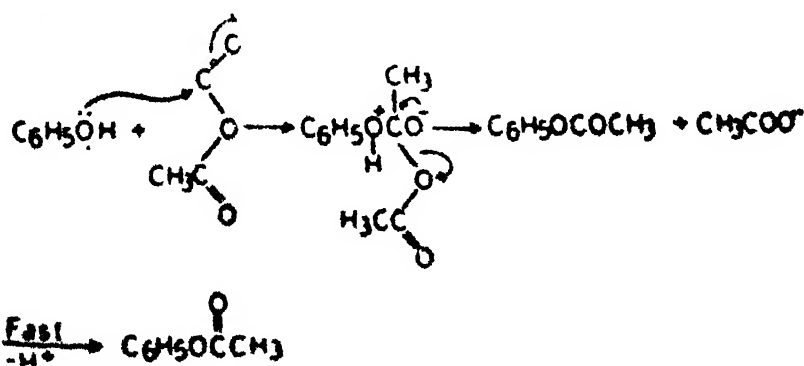


3. Acetylating agents such as acetic anhydride and acetyl chloride form phenyl acetate.

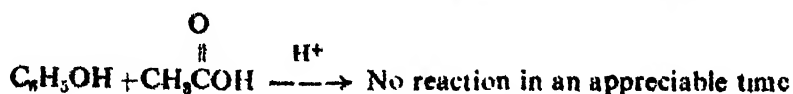


Mechanism

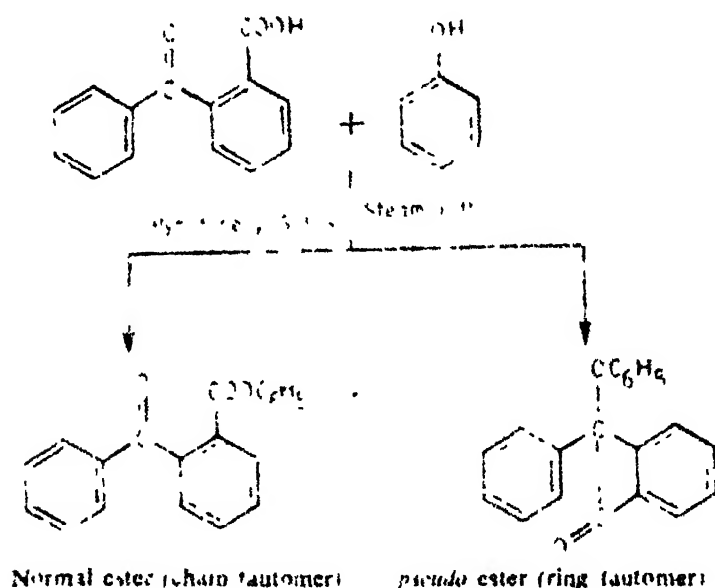
Like the many reactions, we have studied earlier, phenol makes a nucleophilic attack on the acyl carbon atom.



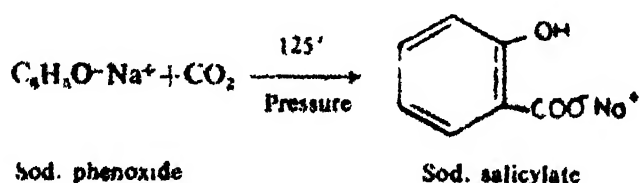
4. **Esterification:** Phenol do not undergo the usual *Fischer esterification* as do alcohols as the equilibrium generally lies towards the left.



Phenols may be esterified in the presence of a carboxylic acid by heating with a mixture of thionyl chloride and pyridine. An interesting reaction is with *o*-benzoylbenzoic acid, which forms two products a normal ester and the *pseudo* ester. the former is formed in a very small amount. This is an example of *ring-chain tautomerism*; the two isomers possess different properties, but on acid hydrolysis both generate the original *o*-benzoylbenzoic acid.

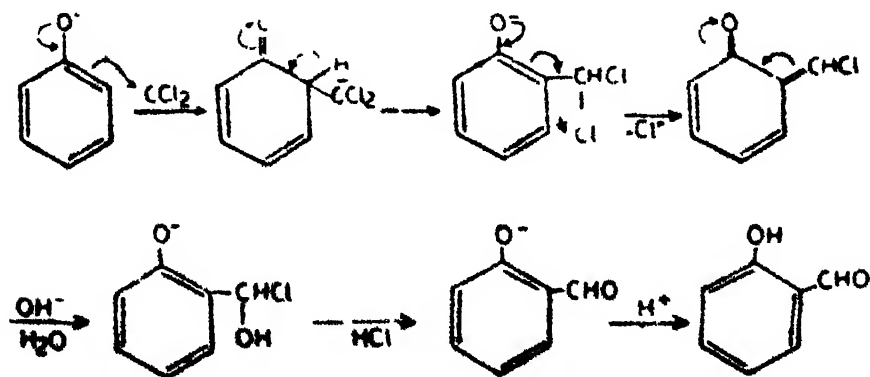


5. **Kolbe's Reaction:** A useful aromatic substitution that involves a phenol and carbon dioxide is Kolbe's reaction. On heating sodium phenoxide under pressure with CO_2 , sodium salicylate is obtained, which is acidified to give salicylic acid

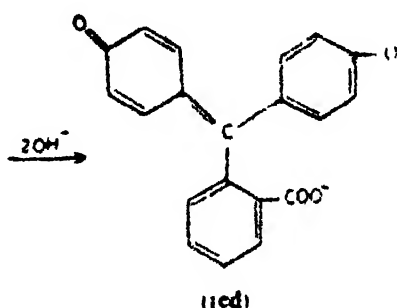
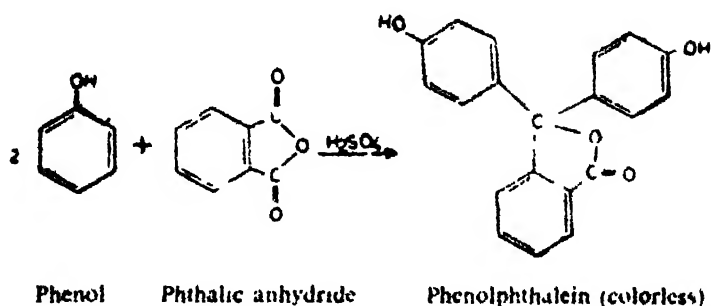


Mechanism

An acceptable mechanism for the Kolbe's reaction consists of the following steps in which CO_2 functions as an electrophile.

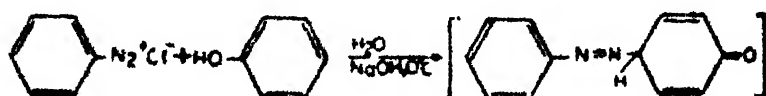


7. Condensation with Phthalic Anhydride: Phenols undergo a special Friedel-Crafts acylation with phthalic anhydride and sulfuric acid to form compounds known as phthaleins.

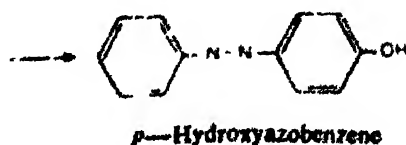


Phthaleins are an important class of indicators as well as dyes. Phenolphthalein, for instance, is colorless in the lactone form below pH 8.5, but above pH 9, i.e., in basic medium an intensely red colored dianion is formed.

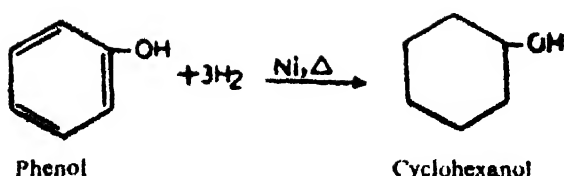
1. Diazonium Coupling: Phenols couple with diazonium salts in basic solution. The reaction presumably involves an electrophilic attack of a weak electrophile on the activated aromatic ring of the phenoxide ion present in alkaline solution.



Benzene diazonium chloride

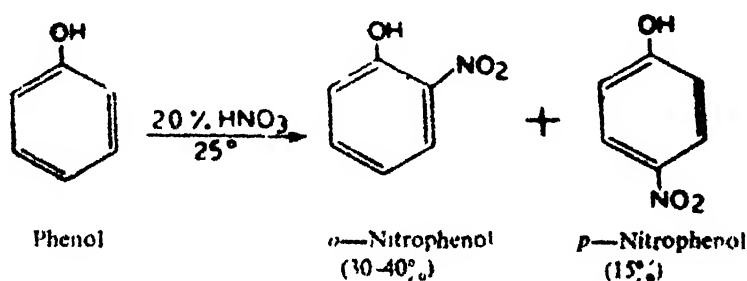


9. Reduction of the Aromatic Ring: Phenolic properties are destroyed when the ring is reduced with H_2 in the presence of Ni, to give cyclohexanol.

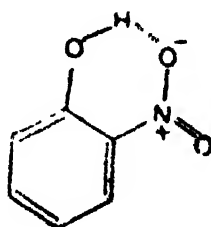


10. Ring Substitution: Electrophilic aromatic substitution on phenol is rather facile because of the powerful activating affect of the —OH group. In contrast the —OR group is less powerful an activator than —OH. The reaction takes place on unionized phenol and *ortho* and *para* derivatives are obtained.

a. **Nitration:** Phenol can be nitrated in dilute aqueous nitric acid even at room temperature and both *ortho* and *para* nitrophenols are formed.



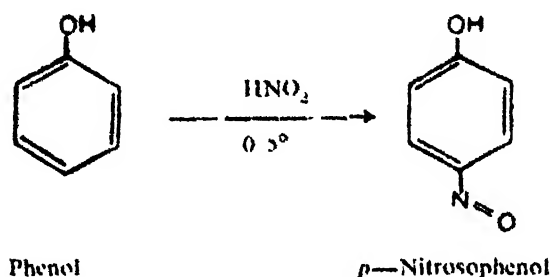
The isomeric compounds in the mixture are separated by steam distillation. *o*-Nitrophenol has a lower solubility in water but a high volatility because of intramolecular hydrogen-bonding



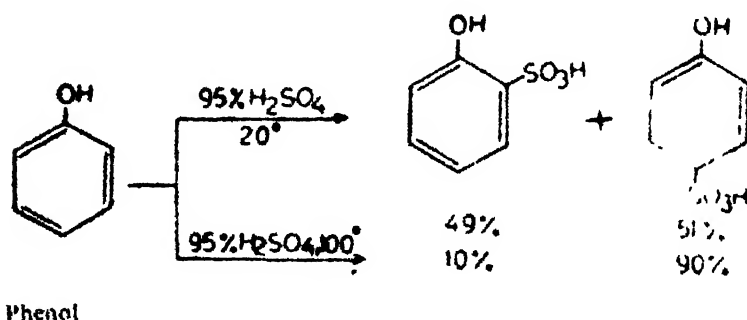
The lower solubility of *o*-nitrophenol is explained by the fact that the hydroxyl group is not available for hydrogen-bonding with water. The acidity of nitrophenols is as follows:

	K_a
<i>o</i> -Nitrophenol	6.8×10^{-8}
<i>m</i> -Nitrophenol	5.3×10^{-8}
<i>p</i> -Nitrophenol	6.5×10^{-8}
2,4-Dinitrophenol	8.5×10^{-8}

b. **Nitrosation:** Phenols can be readily nitrosated at low temperature in the presence of nitrous acid, *p*-nitrosophenol is the major product.

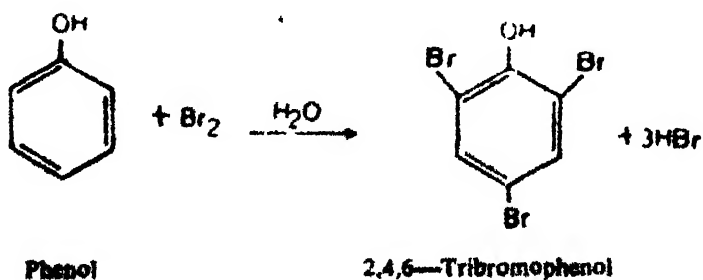


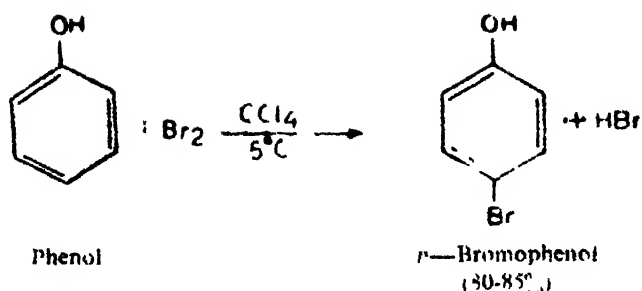
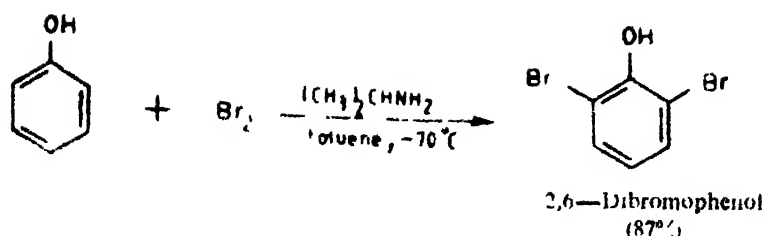
c. **Sulfonation:** Phenol reacts with conc sulfuric acid to form monosulfonated products. The isomeric ratio depends on the temperature of the reaction



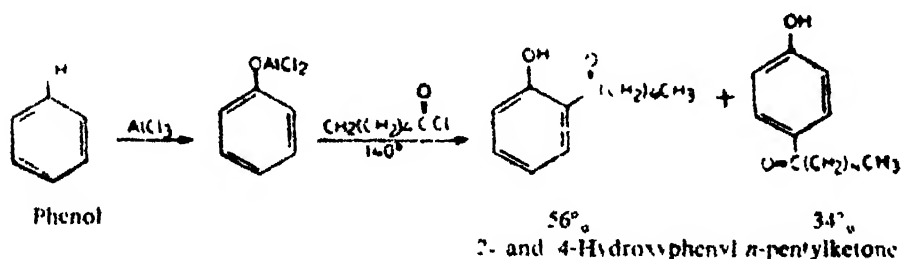
At higher temperature predominantly *p*-isomer is formed because it is of lower energy, compared to the *ortho* isomer due to steric interference of the bulky sulfonic acid group.

1. **Halogenation:** Phenols are readily brominated in an aqueous solution form 2,4,6—tribromophenol. Mostly *p*—bromophenol is obtained by treatment of phenol with bromine in CCl_4

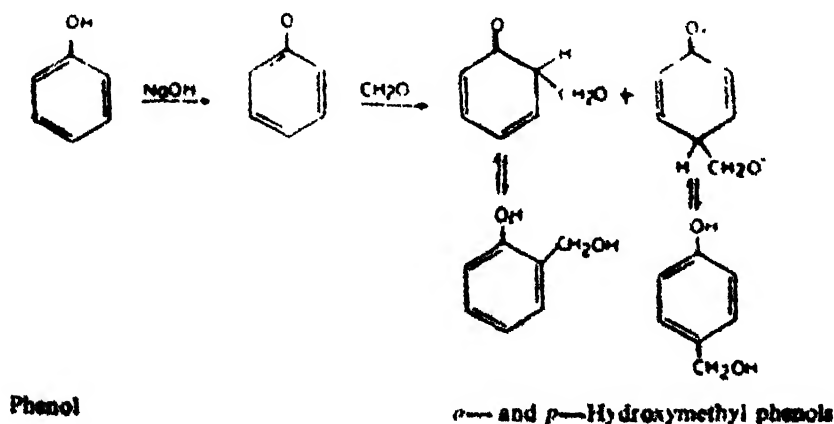




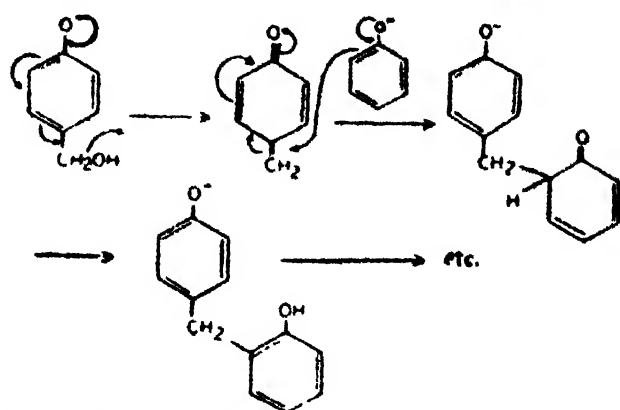
e. *Friedel-Crafts Reaction* Friedel-Crafts alkylation results in alkylation of phenol. Phenol itself reacts with aluminum chloride to form phenoxy-aluminum dichloride salt. This salt on heating in the presence of an acyl chloride leads to acylation products.



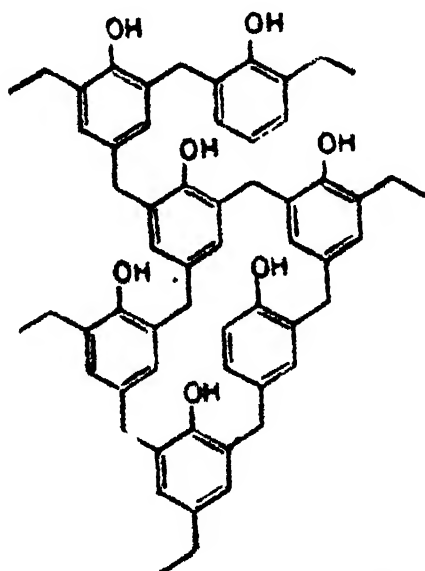
II *Formation of Resins* Formaldehyde condenses with phenol in the presence of alkali in a way which is similar in some respects to aldol condensation.



The *p*-isomer reacts further with phenol in the following manner.

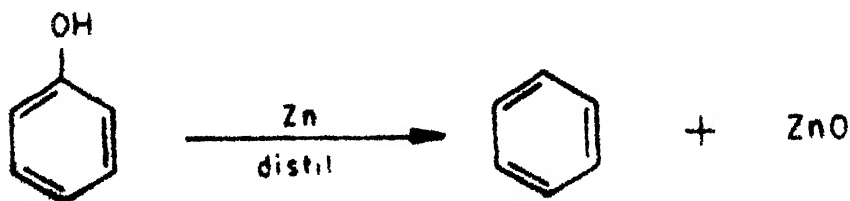


This process repeats over and over again to form the final phenol-formaldehyde resin known as *Bakelite*. The partial structure of the resin is shown below:



Bakelite is a thermosetting plastic and is used in making radio and telephone equipments.

12. On heating phenol with zinc, benzene distils over leaving solid zinc oxide behind.

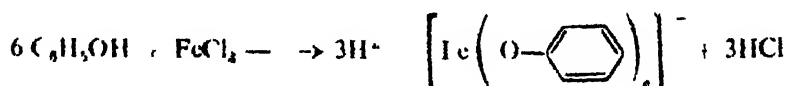


14.23 USES OF PHENOLS

Phenol in a dilute aqueous solution is used as antiseptic and disinfectant, as a raw material for the manufacture of bakelite and for the manufacture of several chemicals such as phenolphthalein, picric acid and cyclohexanol. It is also used in the manufacture of dyes and aspirin. Certain phenols such as 2,6-di-*t*-butylphenol and hydroquinone are used as inhibitors. Phenol is a constituent of cuticura ointment which is often used for the treatment of skin marked by itching.

14.24 QUALITATIVE TEST FOR PHENOLS

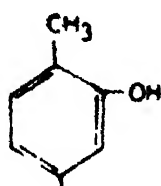
Phenols are weakly acidic and thus soluble in strong bases such as NaOH. They also give colored solution with 5% FeCl₃ solution. Formation of a ferric complex takes place.



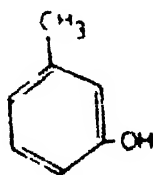
The reaction is favored in polar solvents. Formation of phthaleins between a phenol and phthalic anhydride has already been described on p. 359.

14.25 CRESOLS

Cresol (Isol) is the common name for the methyl derivatives of phenol. These occur in the middle oil fraction of coal tar. The three isomeric cresols have the following structures:



o-Cresol
b.p. 191°



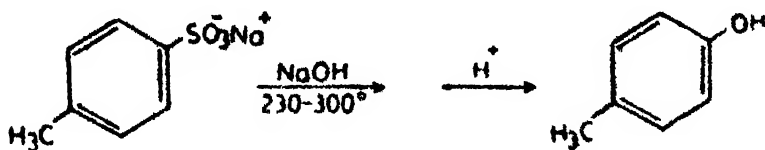
m-Cresol
201°



p-Cresol
225.5°

Preparation

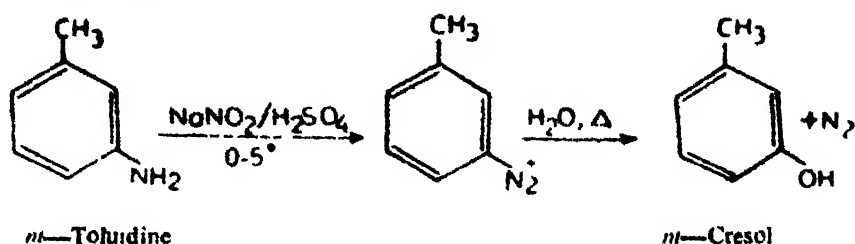
1. Sodium *p*-toluenesulfonate, on fusion with NaOH and subsequent acidification, yields *p*-Cresol.



Sod. *p*-toluenesulfonate

p-Cresol

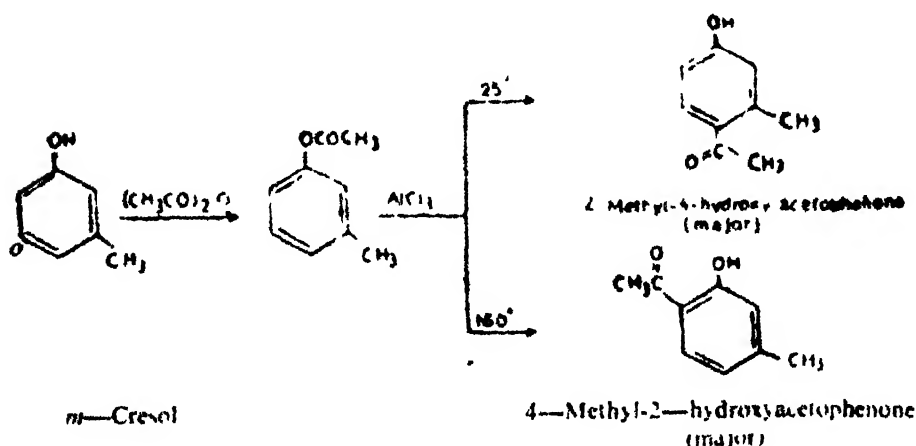
2. Diazotization of *m*-toluidine and subsequent reaction with water results in *m*-cresol.



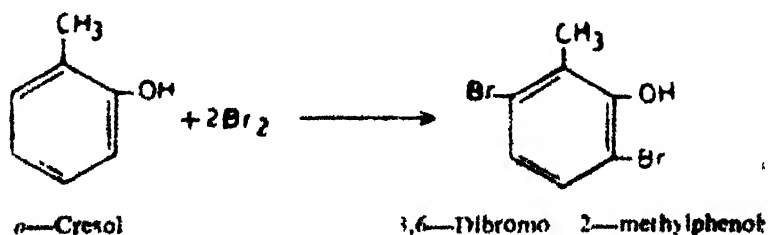
The *o*-isomer is obtained similarly from *o*-toluidine.

Reactions

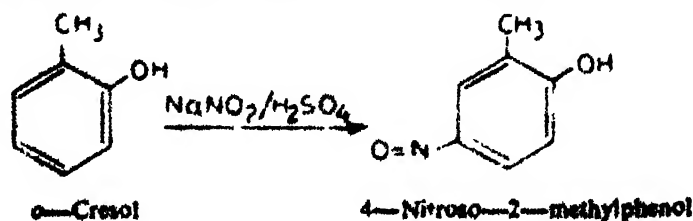
1. *Fries-Rearrangement*: Acetylation of *m*-cresol yields *m*-cresyl acetate which undergoes Fries rearrangement



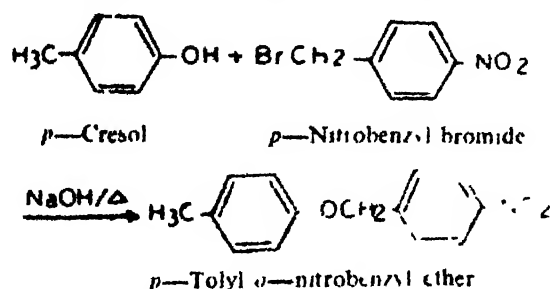
2. *Electrophilic Substitution*. *ortho*-Cresol can be readily brominated in aqueous bromine solution.



3. *o*-Cresol forms nitrosation product with nitrous acid.



4. **Ether Formation:** An ether results from the reaction of *p*-cresol and *p*-nitrobenzyl bromide in the presence of dilute sod. hydroxide.



Uses

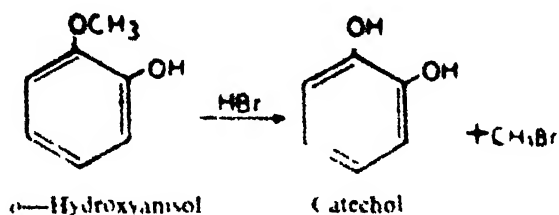
Cresols are used as disinfectants and in the synthesis of industrial chemicals

14.26 CATECHOL

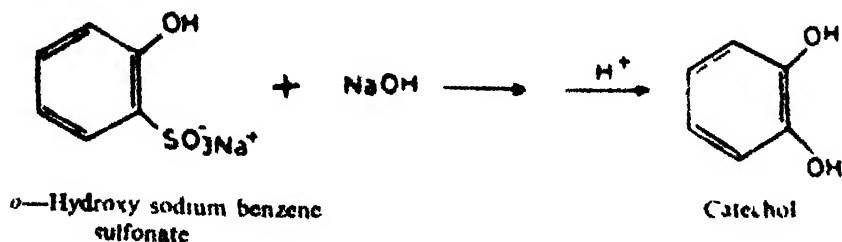
Catechol is *o*-dihydroxybenzene

Preparation

1. Catechol is prepared by the cleavage of the ether linkage of *o*-hydroxyanisole with HBr



2. A convenient synthesis of catechol is the fusion of the sodium salt of *o*-hydroxybenzenesulfonic acid with NaOH and subsequent acidification

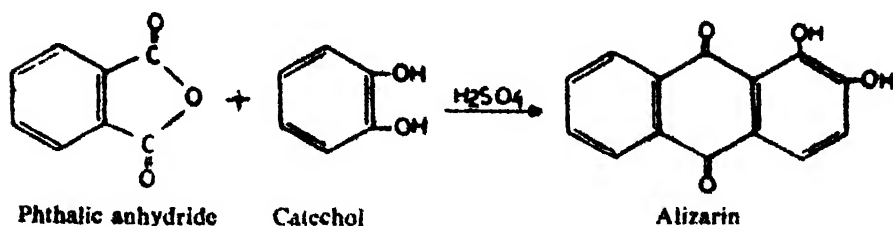


Reactions

1. Catechol is readily oxidized by Ag_2O in ether to *o*-benzoquinone



2. Catechol condenses with phthalic anhydride in the presence of sulfuric acid to form alizarin, a dye.



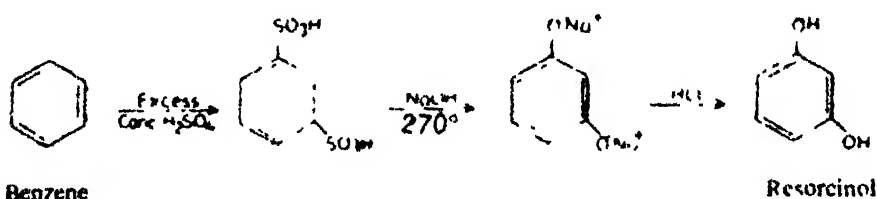
Uses

Catechol is used in the preparation of alizarin and as an oxidant in gasoline.

14.27 RESORCINOL.

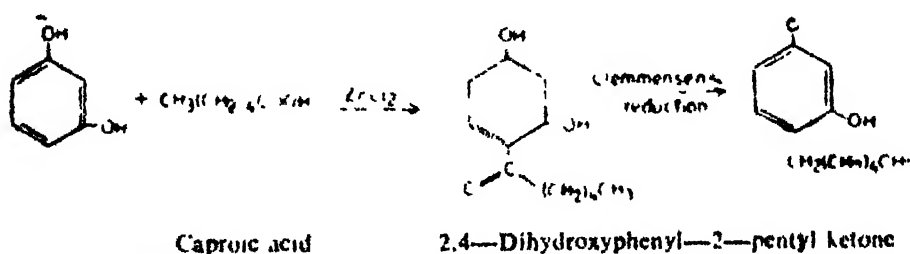
Preparation

1. Benzene, on disulfonation with hot conc. sulfuric acid, produces *m*-benzenedisulfonic acid and resorcinol is obtained on fusion with NaOH of the sodium salt of the acid



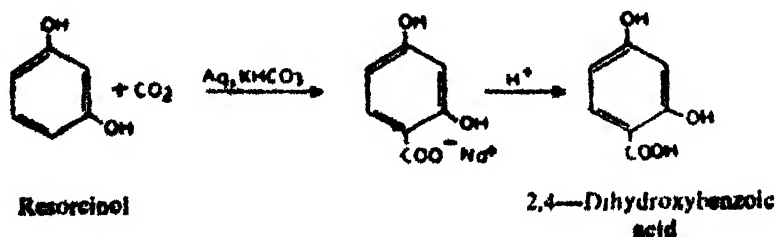
Reactions

1. Resorcinol undergoes F.C. acylation in the presence of a mild catalyst such as ZnCl_2 .

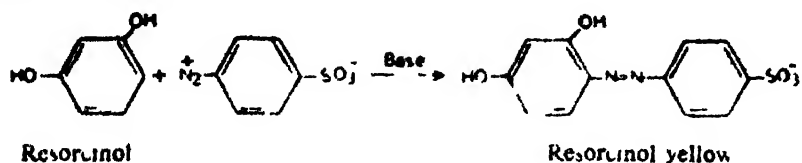


On Clemmensen reduction it yields 4-*n*-hexylresorcinol.

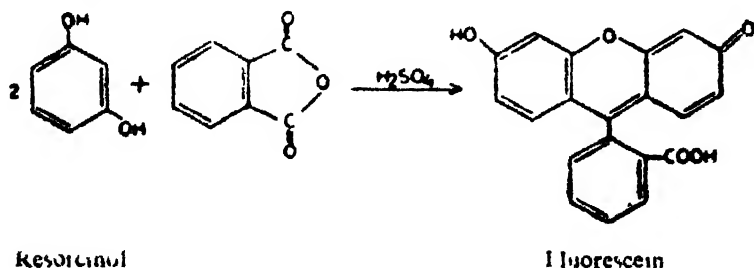
2. *Kolbe's Synthesis*: With CO_2 in basic solution resorcinol forms a carboxylic acid.



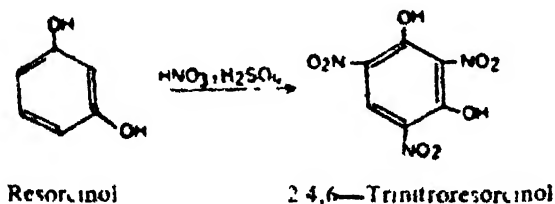
3. Resorcinol condenses with diazotized sulfanilic acid to form *resorcinol yellow*, a dye.



4. Condensation of resorcinol with phthalic anhydride in the presence of sulfuric acid gives an intense fluorescein dye.



5. Resorcinol with conc. nitric acid and sulfuric acid yields a trinitro derivative



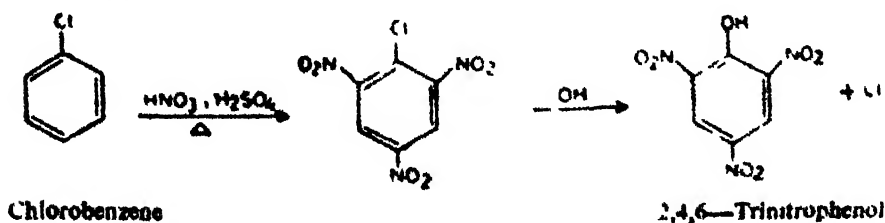
Uses

Resorcinol is used in the preparation of dyes and its derivative hexylresorcinol is used as an antiseptic.

14.28 PICRIC ACID (2,4,6—Trinitrophenol)

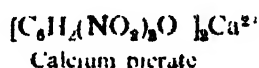
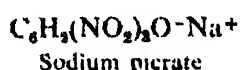
Preparation

1. Picric acid cannot be prepared by nitration of phenol as numerous oxidation products are obtained. A possible route is nitration of chlorobenzene to give trinitrochlorobenzene followed by its hydrolysis with NaHCO₃ solution.



Reactions

Picric acid forms yellow crystals, m.p. 123° and has a bitter taste. It is a very strong acid because after the loss of the proton the oxyanion is highly stabilized by resonance. The hydroxyl hydrogen can be replaced by a metal and the resulting picric acid salts are called *picrates*.



Picric acid also forms adducts with aromatic hydrocarbons of the charge-transfer type. These are intensely colored substances and are used in the identification of aromatic hydrocarbons.

QUESTIONS

14.1 Write short notes on the following:

Absolute alcohol, destructive distillation of wood, power alcohol
Reimer-Tiemann reaction, acidity of phenols and fermentation.

14.2 How would you distinguish between the following pairs?

- a. *o*-Cresol and benzyl alcohol
- b. Phenol and cyclohexanol
- c. Ethyl alcohol and methyl alcohol
- d. 1-Pentanol and 3-pentanol
- e. 1-Propanol and phenol

14.3 Write structural formulas for all the isomeric alcohols of formula $\text{C}_9\text{H}_{19}\text{OH}$ and suggest their IUPAC names.

14.4 Write the products of the reaction of *t*-butyl alcohol with PBr_3 , conc. H_2SO_4 , CH_3COCl , Na , CH_3MgBr , $\text{Na}_2\text{Cr}_2\text{O}_7/\text{H}_2\text{SO}_4$.

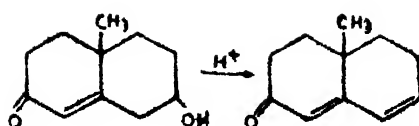
14.5 Write briefly how ethyl alcohol can help alleviate the energy crisis.

14.6 Arrange the following alcohols in order of ease of dehydration.



14.7 Offer explanation for the following observations:

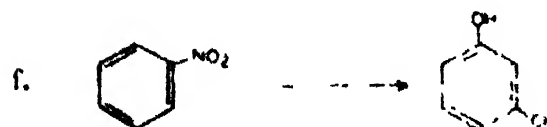
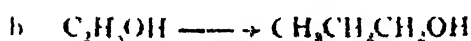
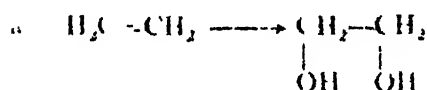
- a. Why is phenol unstable in the keto-form?
- b. The following dehydration is extremely facile.

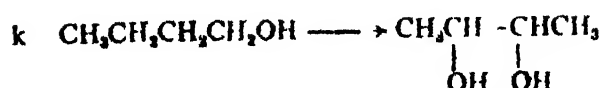
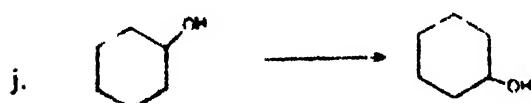
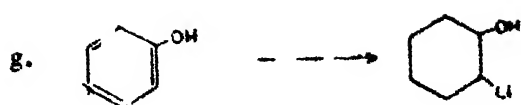


- c. Why does thionyl chloride provide alkyl chlorides of high purity?
- d. 2-Methyl-2-pentanol dehydrates faster than 2-methyl-1-pentanol.
- e. Phenol is acidic but ethyl alcohol is neutral
- f. Ethanol responds to iodoform but tert. butanol does not
- g. A tertiary alcohol reacts faster than a primary alcohol in the Lucas test.
- 14.8 Illustrate by writing chemical equations how ethyl alcohol and phenol differ or behave similarly towards the following reagents:

K, NaOH, PBr_3 , HBr, PCl_5 , SOCl_2 and $\text{CH}_3\text{COOH} \cdot \text{H}^+$

- 14.9 How will you effect the following conversion?





14 10 Postulate a mechanism for the following reaction



14 11 a Why does ethylene glycol have a higher boiling point than dimethyl ether?

b How would you convert cyclohexene into 1,6-hexanediol?

14 12 What are phenols and how are they classified? Give two methods for the large-scale preparation of phenol and its uses. How can phenol be converted into *p*-hydroxyazobenzene, salicylaldehyde, and *ortho* acetyl phenol?

14 13 Give the chemical tests for phenolic and alcoholic groups in an organic compound

14 14 Outline a mechanism for the acid dehydration of ethyl alcohol.

14 15 Give two methods for the synthesis of ethylene glycol. What are its physical and chemical properties? Mention its important uses.

14 16 How does glycerol react with a. HI, b. $(\text{COOH})_2$, and c. Conc. HNO_3 .

14.17 Give a detailed stepwise account of:

- The industrial preparation of ethanol from molasses by fermentation.
- Conversion of ethanol into ethylene and iodoform.

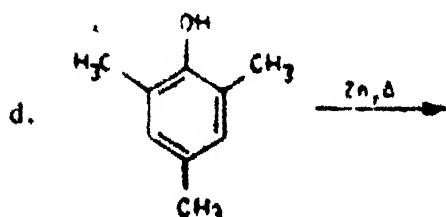
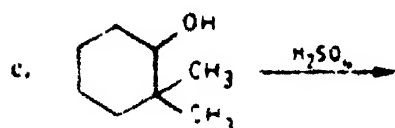
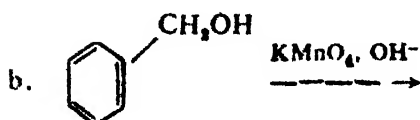
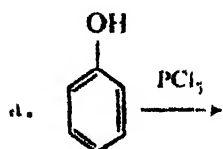
14.18 Describe the industrial preparation of phenol. How can it be converted into:

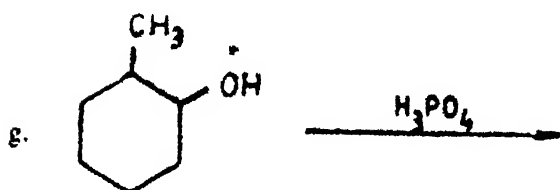
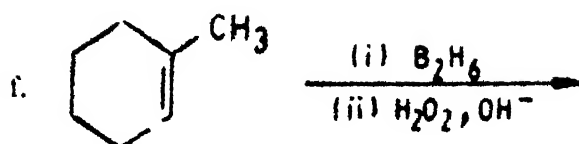
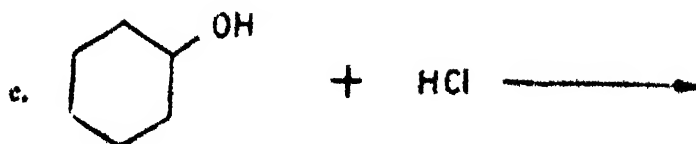
- picric acid.
- salicylic acid and
- phenolphthalein?

14.19 a. How is phenol obtained? How would you convert phenol to (i) benzene (ii) aniline and (iii) cyclohexanol?

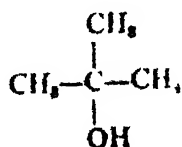
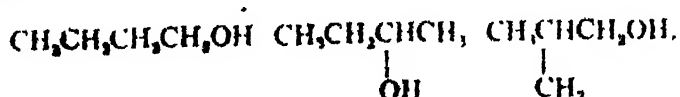
- Suggest the synthesis of isomeric dihydroxybenzenes from any suitable starting materials.

14.20 Predict the product of the following reactions:



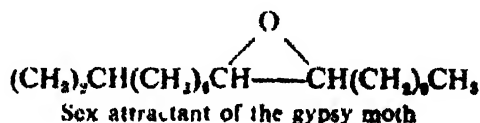
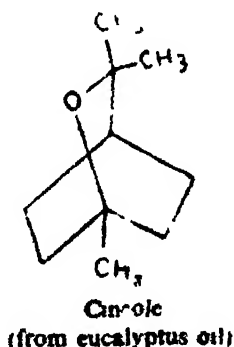
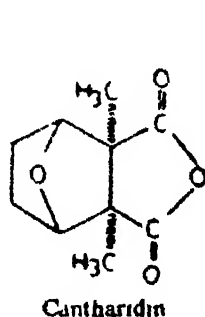


- 14 21 List three methods with pertinent chemical equations for the preparation of alcohols from alkenes.
- 14 22 Dehydration of 3,3-dimethyl-2-butanol leads to two alkenes neither of which is $(\text{CH}_3)_2\text{C}=\text{CH}-\text{CH}_3$. What are their structures?
- 14 23 Which of the following alcohols would react faster with Lucas reagent?



Ethers and Epoxides

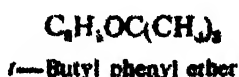
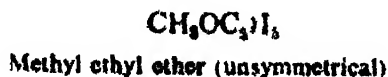
Organic compounds represented by the general molecular formula $R-O-R$ are called *ethers*. They may be represented as alkyl or aryl derivatives of water. *Epoxides* are the cyclic ethers in which oxygen is incorporated into a three-membered ring. As a class, ethers are relatively unreactive but the epoxide ring can be easily cleaved because of angle strain. Ethers may be aliphatic or aromatic and the alkyl groups may be identical or different. An ether linkage is present in many naturally occurring important compounds such as the following.



Ethers may be classified as symmetrical if the two groups are identical and unsymmetrical if the two groups are different.

15.1 NOMENCLATURE OF ETHERS

The common name of ethers is derived by naming the alkyl groups and adding the word ether. The smaller group is written first.





Methyl propyl ether



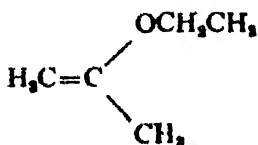
Ethyl ether (Symmetrical)

In naming symmetrical ethers it is not necessary to write the *prefix di*

The IUPAC nomenclature is rarely used. Ethers are named as alkoxy-alkanes. The larger alkyl group is chosen as the stem.



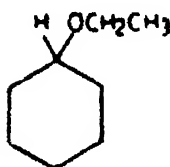
Methoxyethane



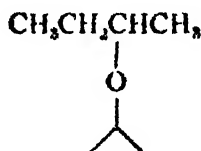
2-Ethoxypropene



Anisole

Ethoxy benzene
(Phenetole)

Ethoxycyclohexane



2-Cyclopropoxybutane

1-Chloro-2,3-epoxy-
propane (Epichlorohydrin)

15.2 PHYSICAL PROPERTIES OF ETHERS

Dimethyl and methyl ethyl ethers are gases whereas ethyl ether and higher homologues of the aliphatic series are liquids. Ethers are weakly polar because the C—O—C bond angle is not exactly 180°. The boiling points are much lower than those of alcohols of the same molecular weight, because the hydrogen-bonding available in alcohols is not possible in ethers since they cannot form hydrogen bonds with each other. The molecules of ethers are thus unassociated with water. Ethers are soluble in water to some extent, for instance, ethyl ether and 2-butyl ether are soluble to the extent of 10 g/100 g of H₂O at 25°. This is because of their capability to form hydrogen-bonds with water.

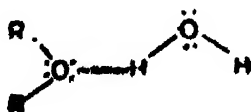


Table 15.1 Physical Constants of Ethers and Epoxides

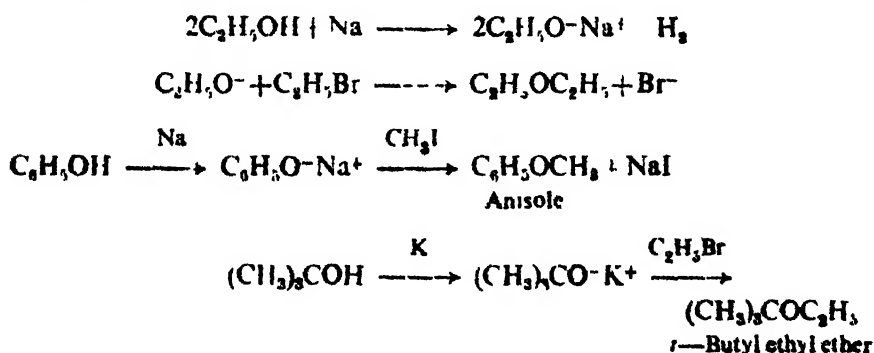
Compound	m.p. (°C)	b.p. (°C)
Methyl ether	-140	24
Ethyl ether	-116	-34.6
<i>n</i> -Propyl ether	122	91
<i>n</i> -Butyl ether	-95	142
Anisole	37	154
Phenetole	-33	172
1,4-Dioxane	11	101
Tetrahydrofuran	-108	66
Ethylene oxide	-111	11

Aromatic ethers, on the other hand, are either liquids or solids. In contrast to alcohols, ethers do not react with sodium metal. Ethers are usually employed as solvents.

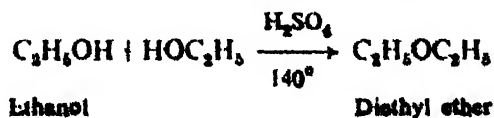
15.3 PREPARATION OF ETHERS

The following general methods may be used for the preparation of ethers.

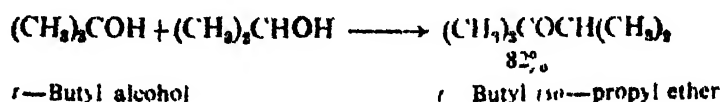
1. *Williamson's Synthesis* This is a general method for the preparation of high molecular weight and aromatic ethers. It can also be adapted to prepare simple and mixed ethers. This procedure involves an S_N2 attack of an alkoxide ion on an appropriate alkyl halide and is illustrated by the following examples.



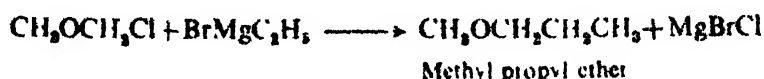
2. *From Alcohols:* This method is used to prepare symmetrical ethers from primary alcohols in the presence of excess conc. sulfuric acid.



Above 140°, i.e. around 180° dehydration of alcohols takes place and secondary and tertiary alcohols undergo dehydration predominantly. An exception to this is in the case of a mixture of alcohols when one alcohol is tertiary and the other primary or secondary because a tertiary carbonium ion is formed readily to yield unsymmetrical ethers.



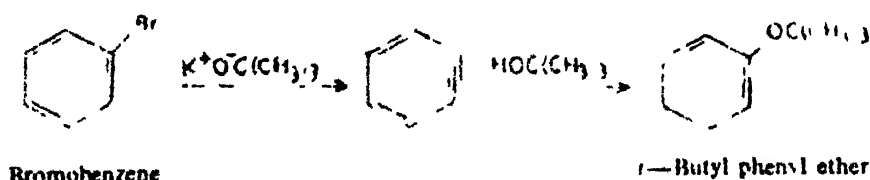
3. *From Grignard Reagents:* An ether may be produced by the action of a Grignard reagent on a halogenated ether



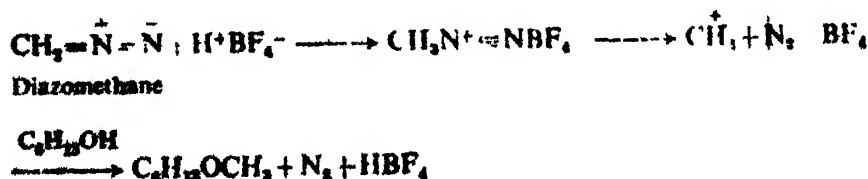
4. Aromatic ethers are obtained from phenol, on reaction with dimethyl or diethyl sulfate



5. *Through a Benzyne Intermediate* t-Butyl alcohol adds to benzyne to produce t-butyl phenyl ether



6. In the presence of fluoroboric acid, diazomethane and alcohols (or phenols) react to give excellent yields of ethers. For example, n-hexyl alcohol is easily converted to methyl hexyl ether by this method



15.4 DIPOLE MOMENT OF ETHERS

If an ether molecule is linear the electric charge in it would be symmetrically distributed around the oxygen atom. The molecule, thus, would have

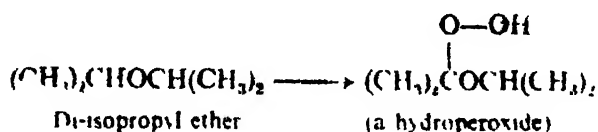
no net dipole moment. But ethers do have dipole moment (for diethyl ether $\mu_D = 1.12$) revealing the angular nature of the molecules. Indeed, the bond angle in ether is around 118° .



An ether

15.5 REACTIONS OF ETHERS

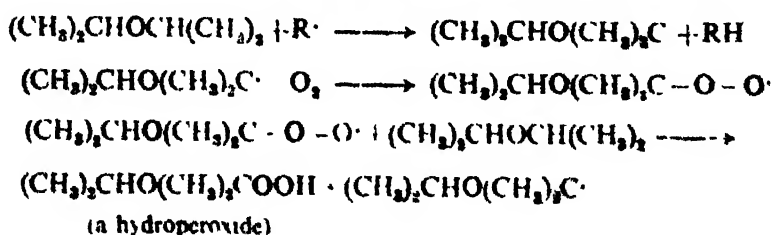
1 *Autoxidation*: Ethers undergo *autoxidation*, i.e., they react with atmospheric oxygen to form peroxides. This is an undesirable reaction of ethers.



All ethers exposed to the atmosphere usually contain peroxides. Peroxides are hazardous because they explode violently on heating. During distillation of an ether, the residue in the distilling flask becomes rich in peroxides, therefore, ethers should not be distilled to dryness. The presence of peroxide in an ether can be detected by shaking a small volume of the ether with aqueous potassium iodide solution. A characteristic purple to brown color appears due to the oxidation of iodide ion to iodine by peroxides.

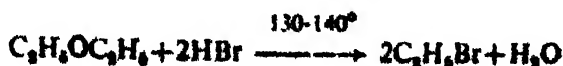
Mechanism

Autoxidation involves the following free radical chain mechanism.



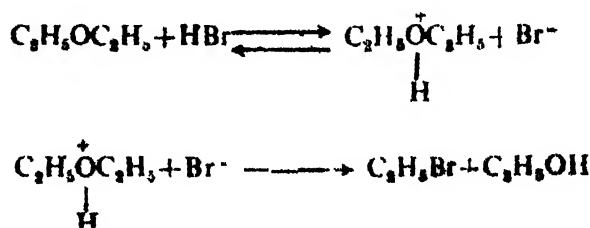
2. *Reaction with Acids*: Ethers as a class are inert toward many reagents. Dilute acids have no effect but ethers are cleaved by strong acids.

a. *Hot Conc. HBr*: Two molecules of alkyl bromide result on boiling an ether with HBr. Initially a molecule of alcohol is also formed which reacts further to form a second molecule of alkyl bromide.

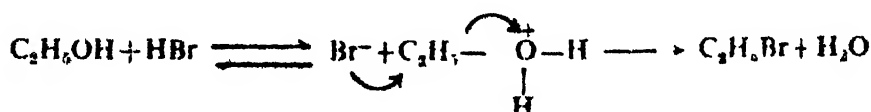


Mechanism

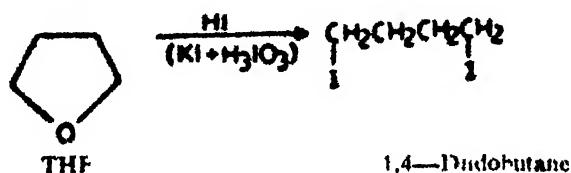
Ether first dissolves in the acid due to its basic nature with the formation of an oxonium ion. This is followed by a S_N2 reaction with the bromide ion functioning as the nucleophile and produces ethyl bromide and ethyl alcohol



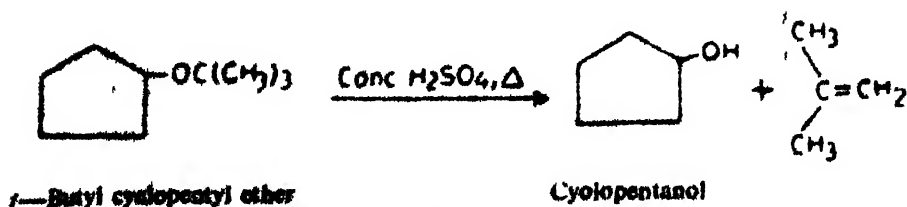
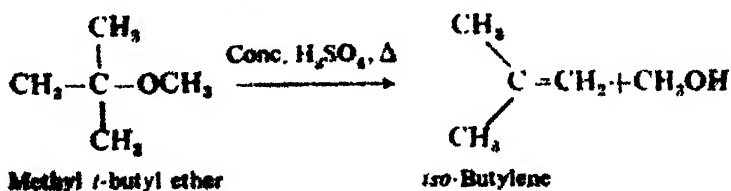
In the next step the ethyl alcohol so formed reacts with HBr to produce a second molecule of ethyl bromide.



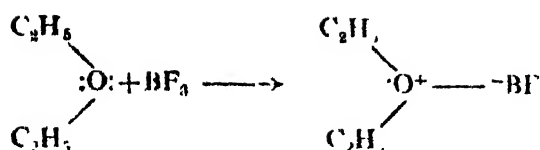
Cyclic ethers are opened by HI or HBr to form the corresponding dihalides



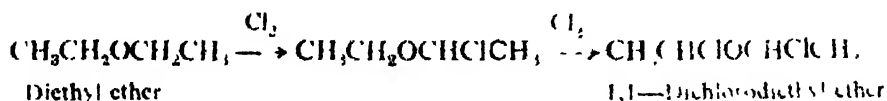
b. *Hot Conc. H_2SO_4* : Secondary and tertiary ethers in hot conc. sulfuric acid form alkenes.



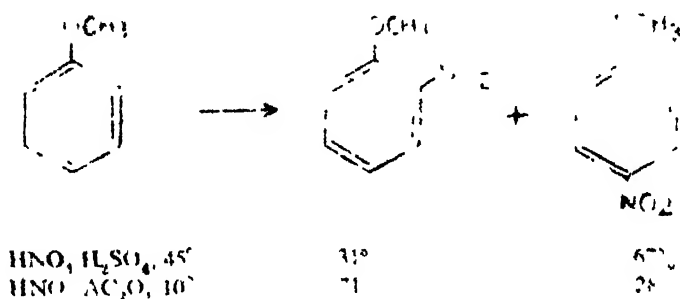
Reaction with Lewis Acids: Because of the unpaired electron on the oxygen atom, ethers form complexes with Lewis acids.



3. **Chlorination:** When an ether is treated with chlorine or bromine, substitution takes place. The hydrogen atom attached to the carbon atom directly linked to the oxygen is the one that is readily replaced. Ether, with chlorine in the dark, yields 1,1-dichlorodiethyl ether



4. **Electrophilic Aromatic Substitution:** Anisole undergoes aromatic substitution in the benzene ring. The $-\text{OCH}_3$ group is less powerful as an activating group than $-\text{OH}$ though it is also *ortho* and *para* directing. The results of nitration of anisole are given below



15.6 USES OF ETHERS

Ethyl ether (simply called as ether) is used medically as an anaesthetic and this was first demonstrated in 1846 by Dr. William Morton of Boston. It is also used as a solvent in the laboratory for Grignard reagents and for extraction of products from organic synthesis. In industry its use is rather limited because of its high inflammability.

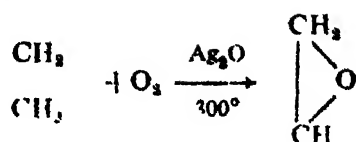
15.7 ETHYLENE OXIDE

Ethylene oxide (IUPAC name oxirane) is a three-membered cyclic epoxide and was first synthesized by Wurtz in 1859. It is, in general, a very useful synthetic intermediate. It is a highly strained ring compound and is easily opened by nucleophilic and electrophilic reagents.

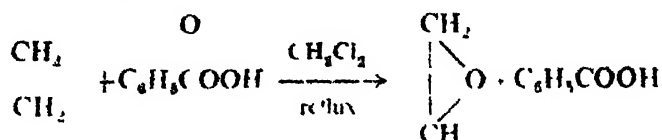
Preparation

1. There are two important commercial processes available for the preparation of ethylene oxide.

a. By direct oxidation of ethylene in the presence of Ag_2O catalyst in a yield of 54%.



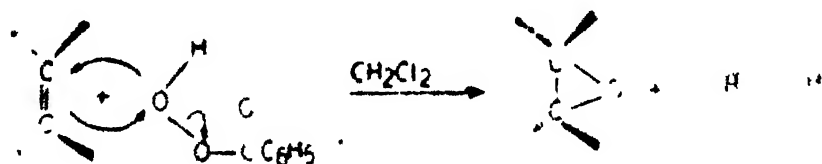
b The second method includes the reaction of alkenes with peracids like perbenzoic, peracetic and *m*-chloroperbenzoic acid, etc. This process is known as *epoxidation*



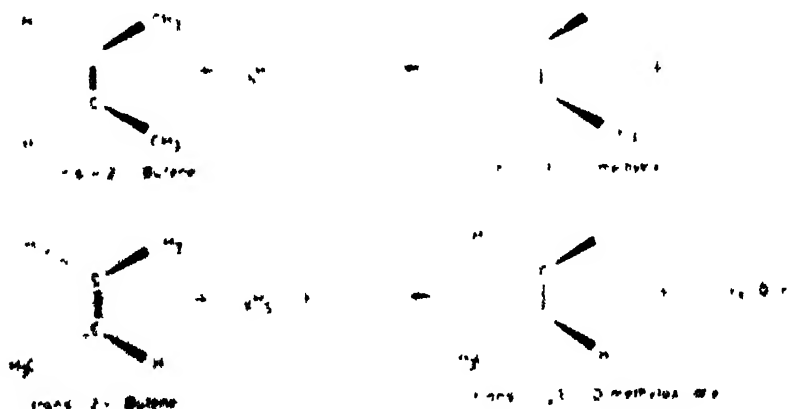
This is the most commonly used method in the laboratory for the preparation of epoxides. Among the various peracids *m*-chloroperbenzoic acid is preferred and is commercially available as a colorless crystalline solid.

Mechanism

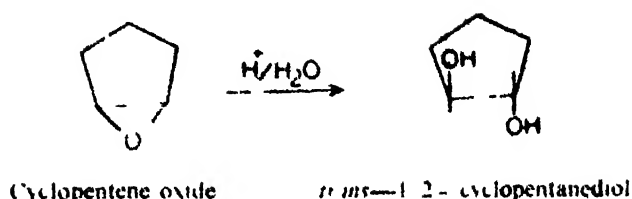
Epoxidation is considered to proceed by an electrophilic attack of the acid on an alkene.



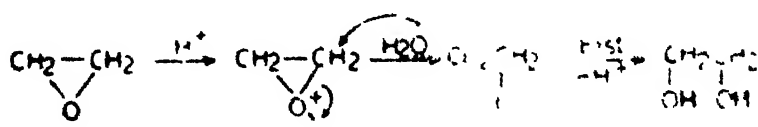
It is a stereospecific reaction and involves a *cis*-addition. Thus a *cis*-alkene yields only a *cis*-epoxide and a *trans*-alkene a *trans*-epoxide. This is exemplified by the epoxidation of isomeric butenes



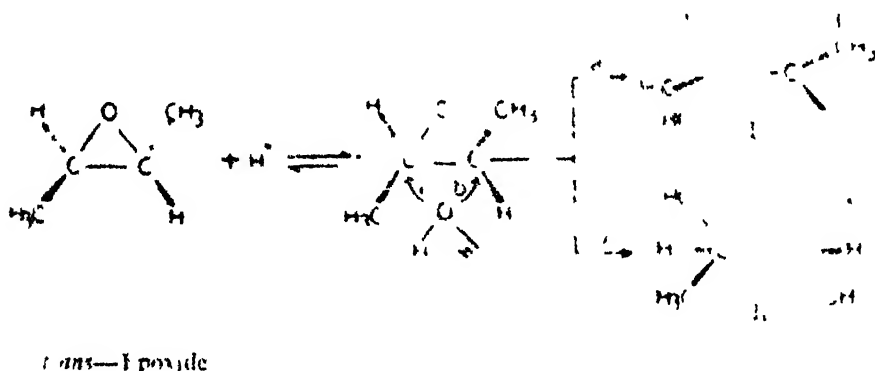
The epoxidation reaction is accelerated if electron-donating groups are present on alkene.

**Mechanism**

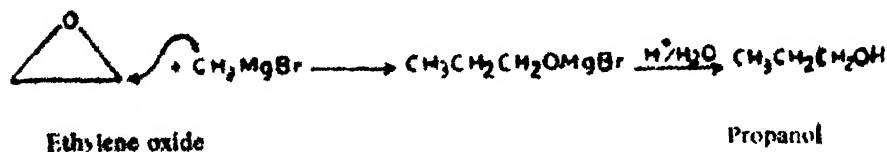
The initial step is the protonation of the oxygen atom to form the oxonium ion. Then attack of a molecule of water and subsequent loss of a proton



yields the product. *trans*-Epoxide opens to form a *meso* glycol while the *cis*-Epoxide affords a *d,l* pair of diol enantiomers. Structures (I) and (II) are identical and represent a *meso* diol

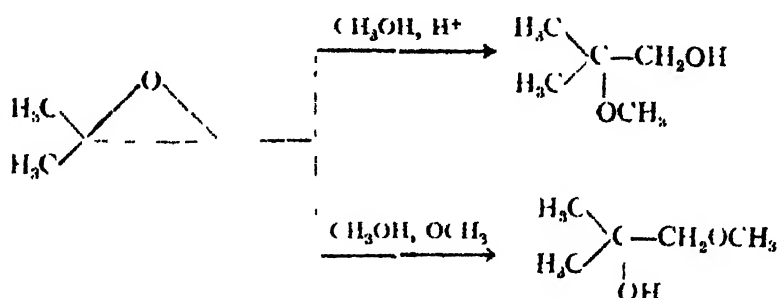


b. The ring may also be opened by methyl lithium or Grignard reagents

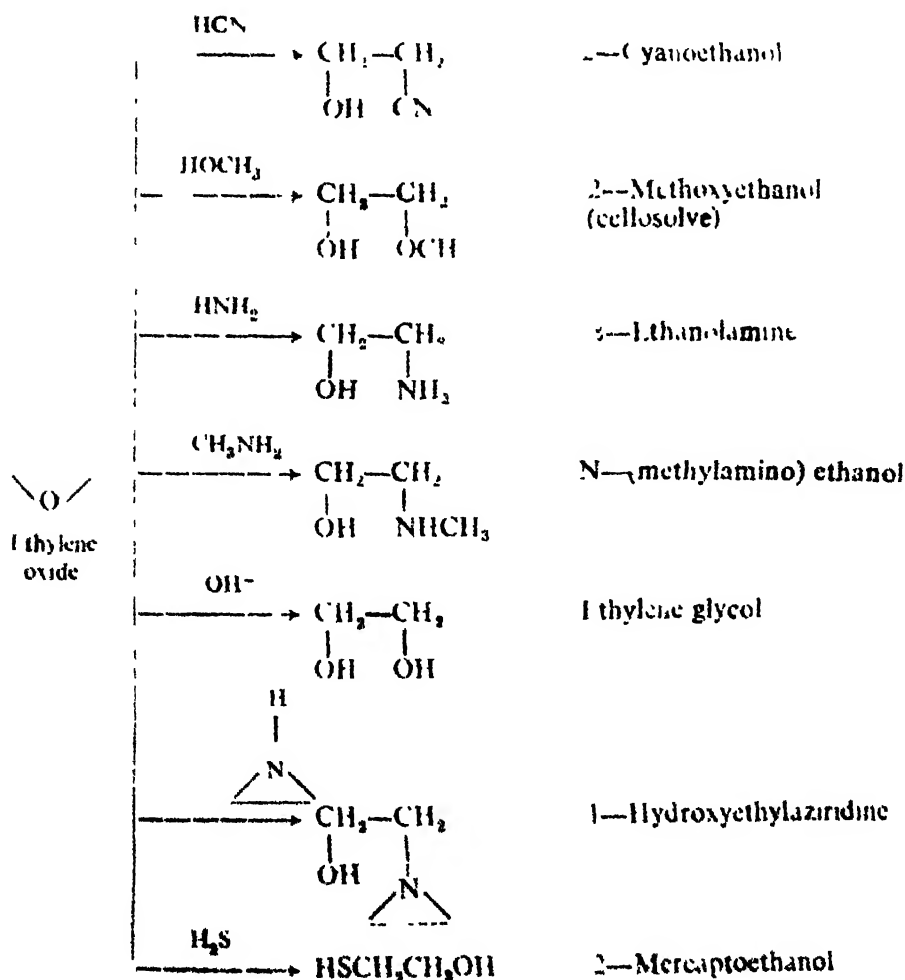


As noticed in the above reactions a symmetrical epoxide can be cleaved by an acid or base by attacking at either carbon atom. However, if the epoxide ring is unsymmetrically substituted then in acid medium the nucleophile attacks the most substituted carbon atom. On the other hand

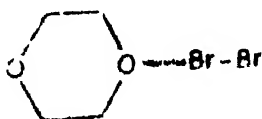
in basic medium the attack by a nucleophile takes place at the least substituted carbon. This is illustrated for the ring opening of 2,2-dimethyloxirane.



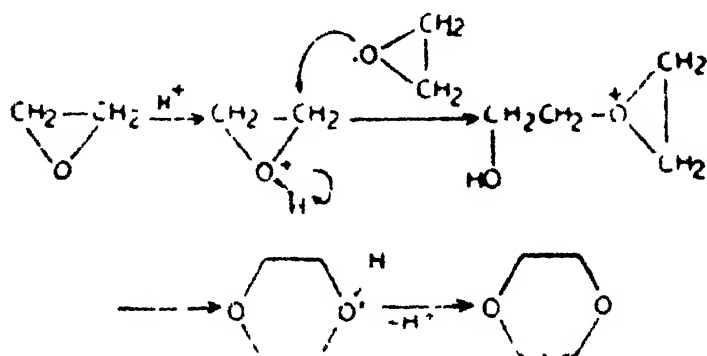
c Several other reagents similarly open the ring, and are summarized below



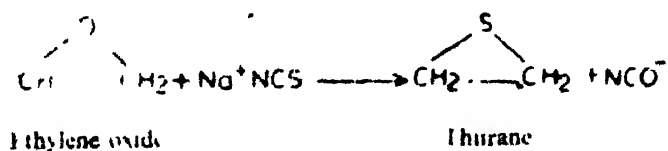
2. Ethylene oxide is thermally unstable and isomerizes to acetaldehyde at 400° . A drop of sulfuric acid dimerizes ethylene oxide to dioxane which with bromine forms dioxane dibromide



Mechanism

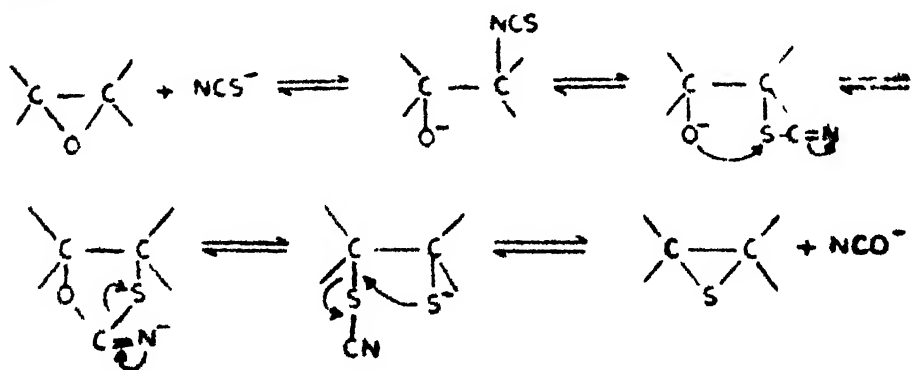


3. The reaction of ethylene oxide with sodium thiocyanate (NaCNS) is accompanied by the formation of thirane, a three-membered ring containing a sulfur atom



Mechanism

The mechanism of this reaction proceeds through a series of equilibrium steps

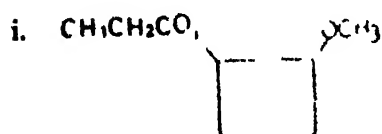
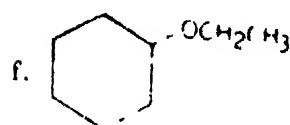
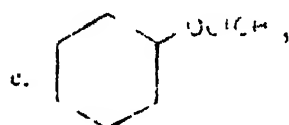
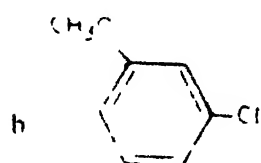
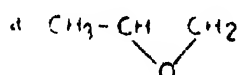


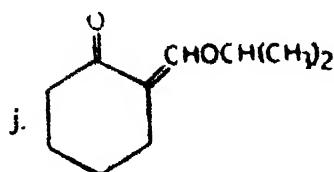
USES

Ethylene oxide is used in the manufacture of solvents (cellosolves, i.e. chemicals which contain both hydroxy and methoxy groups) and as a raw material in the resin industry.

QUESTIONS

15-1 Suggest appropriate names for the following structures





15.2 Explain why  is much more soluble in water than



15.3 What chemical methods can be used to distinguish between the following pairs of compounds

- Methyl ether and ethanol
- Ethoxy ethanol and methyl isopropyl ether
- Butyl iodide and butyl ethyl ether
- Ethyl propyl and ethyl allyl ether
- p*-Methoxyphenol and *p*-methoxybenzyl alcohol

15.4 Write a mechanism for the formation of 1,4-dioxane from ethylene oxide.

15.5 Describe the important preparation and properties of ethylene oxide

15.6 Write the structural formulas for all the isomeric ethers of the formula $C_4H_{10}O$.

15.7 An organic compound with the molecular formula $C_4H_{10}O$ shows the properties of both an alcohol and ether. When treated with excess HBr it yields only ethylene dibromide. Suggest a structure

15.8 An unknown ether is cleaved by HI to give two different alkyl iodides A and B. A contains 89.4% iodine and B contains 81.41% iodine. On hydrolysis with conc pot hydroxide solution B, gives a gaseous hydrocarbon. Suggest a structure for the original ether.

15.9 Write equations for the reaction of $H_2C=CHCH(OCH_3)CH_2OH$ with each



of the following reagents:

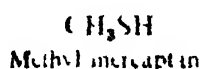
- Excess HBr and heat
- dil $KMnO_4$
- Bromine
- Potassium metal
- Dilute sodium hydroxide

Thiols and Thioethers

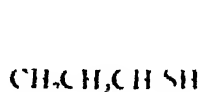
Sulfur analogs of alcohols and ethers are known as thioalcohols or thiols and thioethers respectively. Sulfur is divalent in all these compounds, even though sulfur has various oxidation states besides 2. The prefix *thio* is sometimes used to characterize these compounds.

16.1 NOMENCLATURE

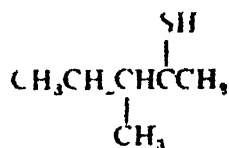
Thiols are commonly called *mercaptans* and a simple thioalcohol is named as mercaptan similar to the alkyl alcohol system of nomenclature.



In the IUPAC system they are called alkanethiol and the alkane name is combined with the suffix thiol.

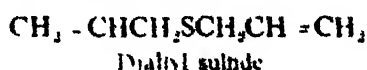
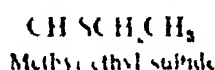
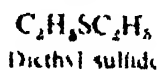


Propanethiol



2-Methyl-2-pentanethiol

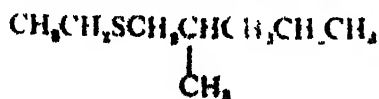
In the trivial nomenclature thioethers are called sulfides and in writing the name the two alkyl groups are followed by the word *sulfide*.



According to the IUPAC nomenclature, thioethers are named as alkylthio alkanes. The prefix *alkylthio* is similar to *alkoxy*- and always refers to the group RS, as in the case of ethers. The larger of the alkyl groups is taken as the stem.



1-(Propylthio) propane



2-Methyl-1-(ethylthio) pentane

16.2 PHYSICAL PROPERTIES OF THIOLS AND THIOETHERS

The sulfur compounds are highly disagreeable to smell. For example, 2-butyl mercaptan ($\text{CH}_3\text{CH}_2\text{CH}(\text{SH})\text{CH}_2\text{CH}_3$) is responsible for the odor of the 'skunk's



defence mechanism. Diallyl sulfide is the chief constituent of oil of garlic and is also present in onions. Thiols and thioethers have boiling points somewhat higher than those of alkanes of corresponding molecular weights. This is accounted for by the intermolecular attraction of molecules of sulfur compounds because of the C—S dipole. Thiols also have lower boiling points than the corresponding alcohols because of weaker intermolecular hydrogen bonding in thiols as the sulfur atom is much less electronegative than oxygen.

Table 16.1 Mercaptans or Thiols

Compound	m.p. ($^{\circ}\text{C}$)	b.p. ($^{\circ}\text{C}$)
Methyl mercaptan	127.1	-6
Ethyl mercaptan	121	34.7
<i>n</i> -Propyl mercaptan	111.5	68
<i>iso</i> -Propyl mercaptan	-130.0	60
<i>n</i> -Butyl mercaptan	115.9	98
<i>iso</i> -Butyl mercaptan	79	88

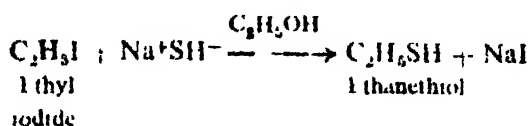
Table 16.2 Sulfides or Thioethers

Compound	m.p. ($^{\circ}\text{C}$)	b.p. ($^{\circ}\text{C}$)
Dimethyl sulfide	-83.2	38
Diethyl sulfide	-102.1	92
Dipropyl sulfide	-101.9	142
Dibutyl sulfide	-79.7	185

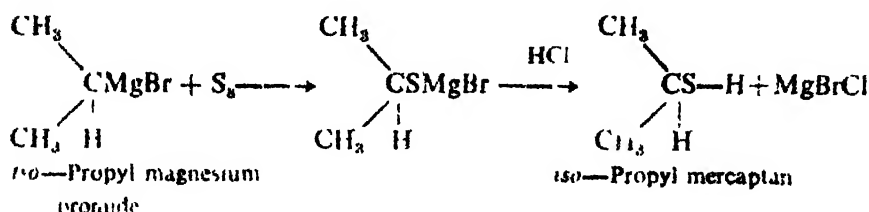
Thioalcohols are less soluble in water than are alcohols.

16.3 PREPARATION OF THIOALCOHOLS

1. On heating an alkyl halide with sodium hydrogen sulfide, the halide group is replaced by *hydrosulfide ion* (SH^-) by a displacement reaction. Ethanol is used as a solvent.

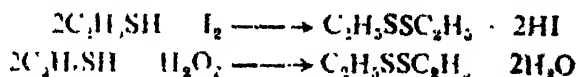


2. Reaction of a Grignard reagent with sulfur yields a thioalcohol.

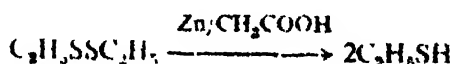


16.4 REACTIONS OF THIOALCOHOLS

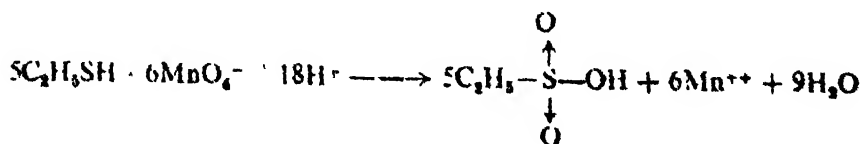
1. *Oxidation*: Thioalcohols are easily oxidized to disulfides and only a mild oxidizing agent such as I_2 , H_2O_2 or CuCl_2 is required.



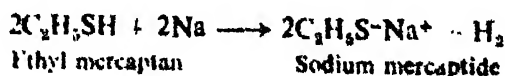
The reverse reaction, i.e., the cleavage of the S—S bond takes place with ease by mild reducing agents.



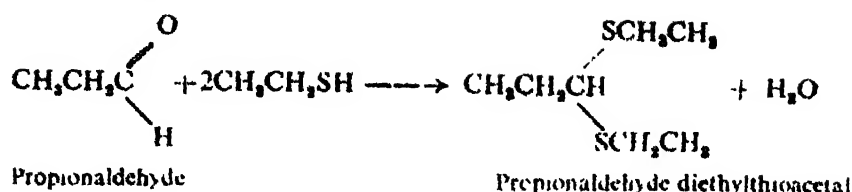
With KMnO_4 (a strong oxidizing agent) a sulfonic acid is obtained



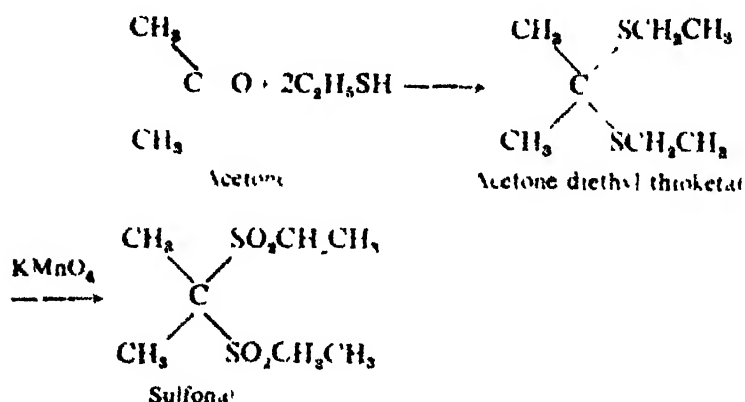
2. Although thiols are weak acids, they form salts with sodium metal.



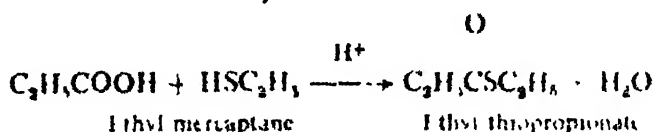
3. *Formation of Thioacetal*: Thiols condense readily with aldehydes to form thioacetal.



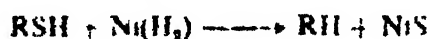
With ketones (acetone) they form ketals which on oxidation yield sulfonal:



4. *Formation of Thioesters:* In the presence of a mineral acid catalyst, thioalcohols react with carboxylic acids to form thioesters



5. *Reductive Cleavage:* With Raney nickel the C—S bond is broken and replaced by C—H: the process is also known as *desulfurization*

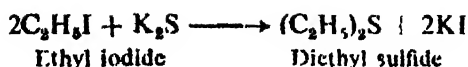


16.5 USES OF THIOALCOHOLS

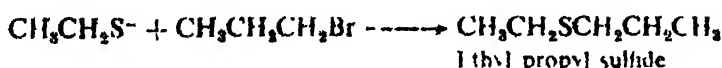
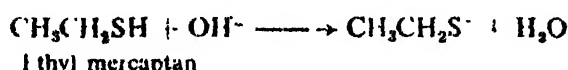
Thioalcohols or mercaptans are used as intermediates in the synthesis of vat dyes and in the preparation of hypnotics (sulfonal). Mercaptans like CCl_4 enter into radical displacement reactions with growing polymer chains and are called chain transfer compounds

16.6 PREPARATION OF THIOETHERS

1. On heating potassium sulfide with an alkyl halide, a thioether is obtained.



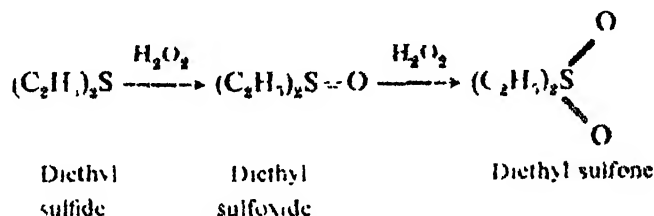
2. $\text{S}_{\text{N}}2$ displacement by alkylthio anion on alkyl halides, similar to Williamson synthesis, results in a thioether



Sulfur compounds display greater nucleophilic reactivity than their oxygen analogues and substitution often occurs under mild conditions.

16.7 REACTIONS OF THIOETHERS

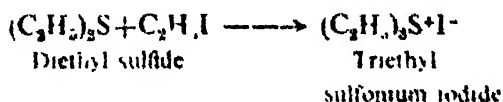
1. *Oxidation* Sulfides are oxidized first to sulfoxides which are converted to sulfones in the presence of oxidizing agents



Other oxidizing agents such as potassium permanganate, nitric acid, etc. bring about similar changes.

Sulfones are neutral crystalline substances and very stable. They are very difficult to reduce.

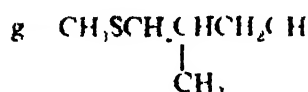
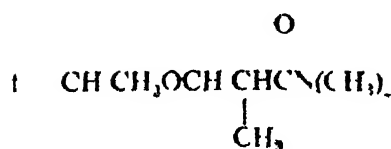
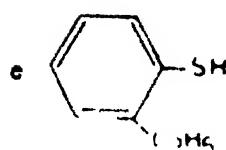
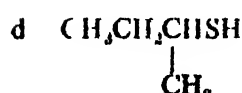
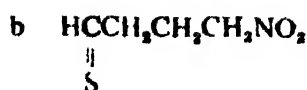
2. *Formation of Sulfonium Salts:* Sulfides react with alkyl halides to form sulfonium salts. These salts on heating decompose back to alkyl sulphide and alkyl halide



3. *Reductive Cleavage:* Analogous to mercaptans, thioethers (or sulfides) are desulfurized with Raney nickel.



4. Unlike ethers, these are decomposed by alkali solutions to form alcohols.

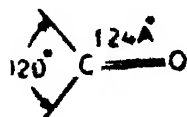


- 16 2 How are mercaptans prepared? Describe their physical and chemical properties. Describe the preparation and uses of sulfonal.
- 16 3 Show the products of the reaction (if any) of 1-butanethiol with I_2 , Na , CH_3COCl , MnO_4^- and $\text{Ni}(\text{H}_2)$.
- 16 4 What classes of products may be obtained by the oxidation of a thiol by different oxidizing agents?
- 16 5 How will you proceed to synthesize mustard gas? Discuss its nucleophilic displacement reaction.
- 16 6 What are mercaptans? How does ethyl mercaptan react with (i) an aldehyde, (ii) an acid chloride, (iii) lead acetate and (iv) hydrogen peroxide?

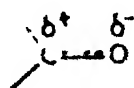
Aldehydes and Ketones

The compounds which contain a carbonyl group (a carbon-oxygen double bond) are collectively known as aldehydes and ketones. In an aldehyde the carbon of the $C=O$ is bonded to H and one organic group, R, while in a ketone it is bonded to two organic groups. These are two important classes of carbonyl compounds which have many reactions in common but have significant differences too. The carbonyl group largely determines the identity of these two classes of compounds. Many compounds containing these functional groups occur in plants and animals, for instance, benzaldehyde (almonds), cinnamaldehyde (cinnamon), testosterone (sex hormone), camphor (camphor tree), vanillin (vanilla), civetone (civet cats), etc.

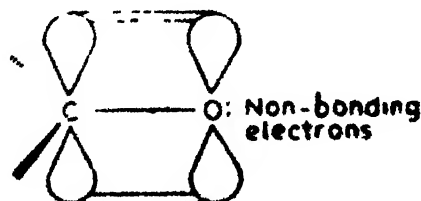
The carbon-oxygen bond in $C=O$ is composed of a σ - and a π -bond similar to alkenes, but instead connecting two atoms of quite different electronegativities. The σ -bond is formed by overlap of carbon sp^2 hybridized



Lewis Structure



Polarized bond



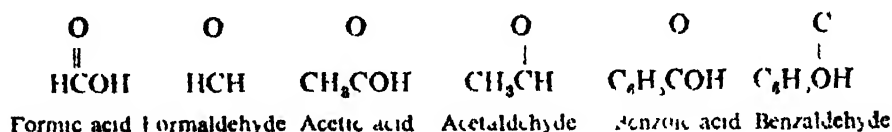
Molecular Orbital Representation

orbital with the p orbital of the oxygen atom. The π -bond is formed by a side to side overlap of a p_x orbital on the carbon atom with a p_x orbital of the oxygen atom as shown. The carbon atom is sp^2 hybridized and the three bonds subtend an angle of 120° , thus all the bonds to the carbon atom lie in the same plane and the $C=O$ bond distance is 1.24\AA . Since oxygen is more electronegative than the carbon atom the shared pair of electrons between them lies closer to the oxygen atom. The $C=O$ bond is thus polarized and because of this the carbon atom develops a positive charge

and is attacked by many ionic reagents. The oxygen atom contains two pairs of non-bonding electrons. The electronic structure of the carbonyl group is responsible for most of the properties of aldehydes and ketones.

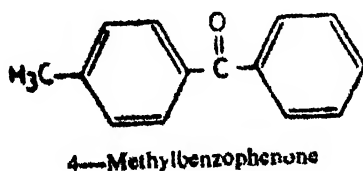
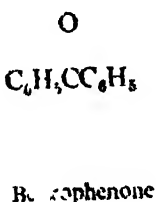
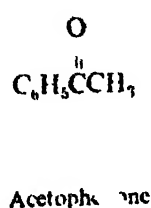
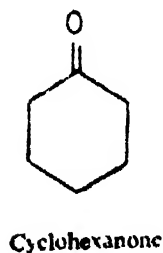
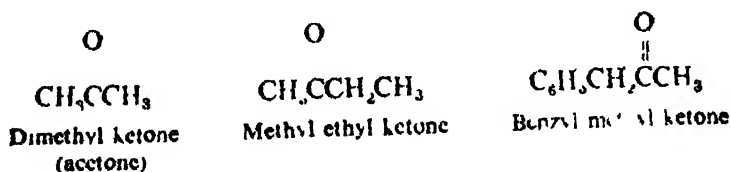
17.1 NOMENCLATURE OF ALDEHYDES AND KETONES

Aldehydes: Aldehydes have a hydrogen atom attached to the carbonyl group. The common name of an aldehyde is derived from the corresponding carboxylic acid by dropping the suffix *-ic* and adding the suffix *aldehyde*. Thus,



These aldehydes are readily oxidized to the carboxylic acids. The $-\text{CHO}$ group is also referred to as the *formyl group*.

Ketones: Ketones have two alkyl or aryl groups. Simple ketone may be named by using the names of the alkyl groups attached to the carbonyl group followed by the word *ketone*.



17.2 PHYSICAL PROPERTIES OF ALDEHYDES AND KETONES

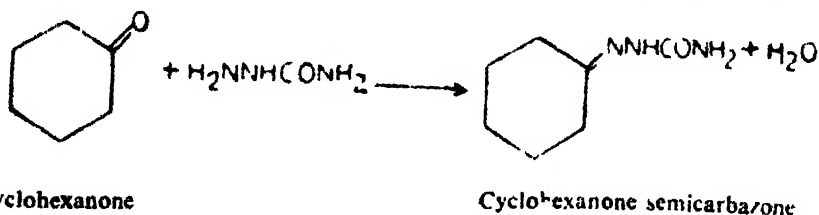
Formaldehyde is a gas, whereas the simpler members are colorless liquids. An aqueous solution of formaldehyde is known as formalin. The boiling points of both aldehydes and ketones increase with increasing molecular weight (Table 17.1). They cannot form hydrogen-bonds with themselves because the hydrogen is attached to the carbon atom as a result they have lower boiling points than the corresponding alcohols or carboxylic acids but possess higher boiling points than hydrocarbons. For example, *n*-butyl alcohol boils at 118°, *n*-butane at 0°, while butyraldehyde boils at 76° only because the carbonyl group is polar. The lower aldehydes and ketones are miscible with water, because the carbonyl oxygen forms strong hydrogen bonds with water but the solubility decreases after about five carbon atoms.

Since the electron pair between carbon and oxygen is unequally shared, as a result aldehydes and ketones have a high dipole moment value, for instance, formaldehyde has a value of 2.27 D and acetone of 2.85 D. Since the π electrons are much more polarized than the σ -electrons, the dipole moment in $\diagup \text{C}=\text{O}$ is greater than in $\diagup \text{C}-\text{Cl}$ bond. The lower members have a penetrating odor but become fragrant smelling with increasing molecular weights.

Table 17.1 Physical Constants of Aldehydes and Ketones

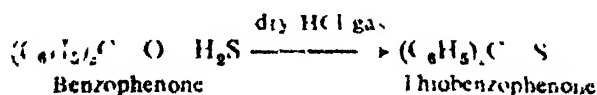
Compound	m.p. (°C)	b.p. (°C)
Formaldehyde	-92	21
Acetaldehyde	121	20
Propionaldehyde	91	49
<i>n</i> -Butyraldehyde	100	76
<i>n</i> -Valeraldehyde	91	103
Caproaldehyde		131
Enanthaldehyde	-42	155
Benzaldehyde	26	142
Salicylaldehyde	2	197
<i>p</i> -Hydroxybenzaldehyde	116	
Anisaldehyde	2	248
Acetone	94	56
Methyl ethyl ketone	86	80
2-Pentanone	78	102
3-Pentanone	-41	101
2-Hexanone	-35	156
Acetophenone	21	202
Propiophenone	21	218
2-Butyrophenone	11	232
Benzophenone	48	306
Cyclopentanone		130
Cyclohexanone		155

d. **Semicarbazone Formation:** A semicarbazide is an amide derivative of hydrazine and reacts with aldehydes and ketones to form semicarbazones.

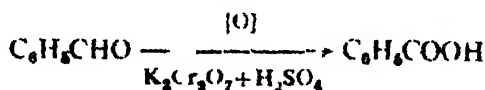
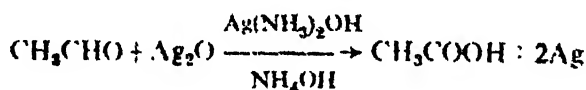


All the above reagents are poor nucleophiles. Therefore, the addition is catalyzed by controlling the pH (5 to 6) of the medium. In an acid medium protonation of the carbonyl oxygen takes place which increases the electrophilic character of the carbonyl carbon atom.

e. **Formation of Thioketones:** Reaction of H_2S with ketones results in the formation of thioketones.

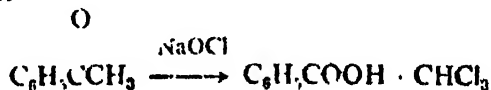


3. **Oxidation.** A marked difference between aldehydes and ketones is the greater ease of oxidation of aldehydes. It requires only a very mild oxidizing agent to oxidize an aldehyde to a carboxylic acid.



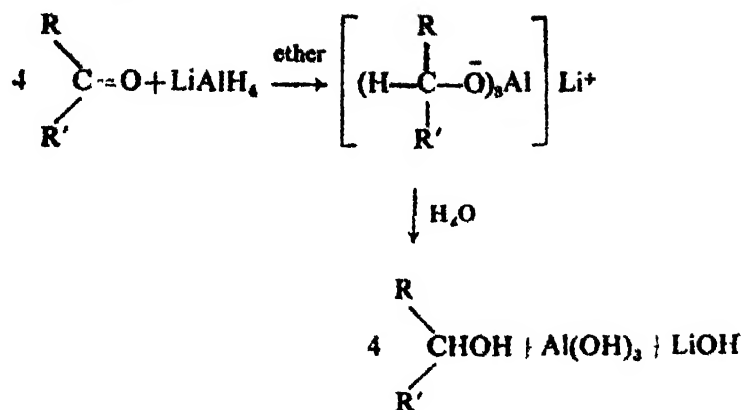
Only methyl ketones are oxidized to carboxylic acids by sodium hypo-

chlorite ($\text{NaOH} - \text{Cl}_2$). It is specific reagent for the oxidation of $\text{—}\overset{\text{O}}{\underset{\text{O}}{\text{C}}}\text{—CH}_3$ grouping to —COOH



4. **Reduction:** Reducing agents such as LiAlH_4 , NaBH_4 and H_2/Ni reduce aldehydes to primary alcohols and ketones to secondary alcohols. Reduction is also an example of addition of hydrogen across the $\text{C}=\text{O}$ bond. LiAlH_4 is handled like Grignard reagents. It is soluble in ether and sensitive to moisture and oxygen.

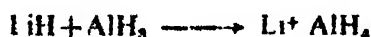




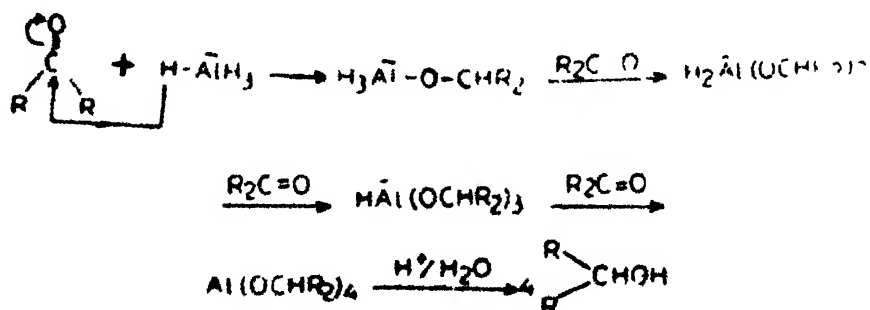
Lithium aluminum hydride is a more powerful reducing agent than sodium borohydride. It reacts readily with water. The reduction with sodium borohydride requires the presence of a polar solvent such as ethanol.

Mechanism

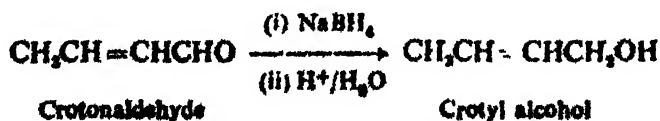
Lithium aluminum hydride may be regarded as derived from a metal hydride:

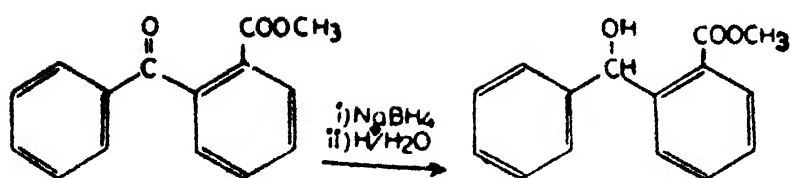


The anion is a nucleophile and can attack the polarized carbonyl carbon atom.

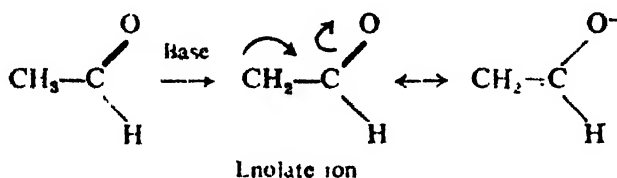


Lithium aluminum hydride not only reduces aldehydes and ketones but reduces esters, acids and nitriles as well. Sodium borohydride in contrast, is a selective reducing agent and reduces aldehydes and ketones only, but not carboxylic acids and esters. Sodium borohydride also does not attack the C=O and C=C bonds in a compound.

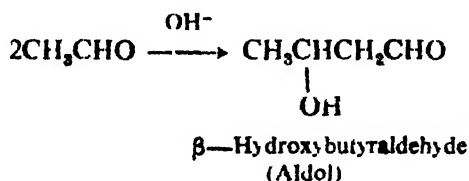


Methyl *o*-benzoylbenzoate*o*-Carbomethoxydiphenyl methanol

5. **The Aldol Condensations:** A carbon atom located next to a carbonyl carbon is referred to as the α -carbon and a hydrogen attached to an α -carbon is called an α -hydrogen. This hydrogen is acidic due to the fact that the anion, also known as the *enolate ion*, is stabilized by resonance in the manner shown below:

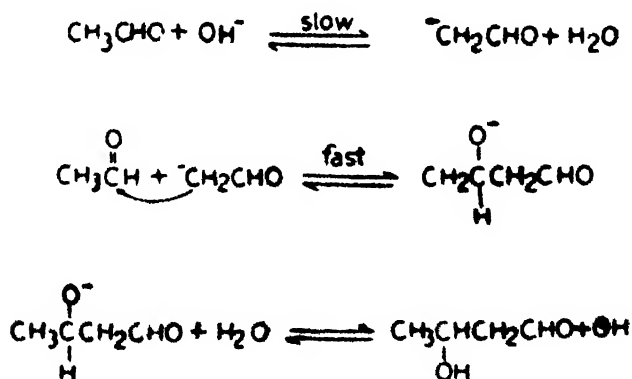


The enolate ion is the intermediate in the aldol condensation of aldehydes and ketones. Acetaldehyde, for instance, forms a dimeric product aldol in the presence of a dilute base (10%, NaOH).



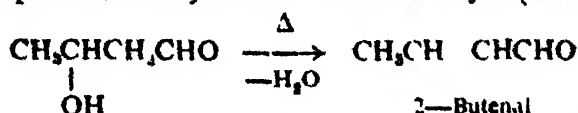
Mechanism

The formation of the aldol proceeds through a series of equilibrium steps.

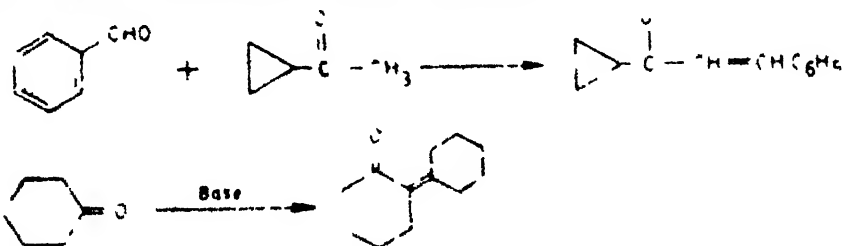


A hydroxide ion pulls an α -hydrogen from acetaldehyde and the resultant enolate ion makes a nucleophilic attack on a second molecule of acetaldehyde in a fast step. This ion then picks up a proton from water to form an aldol and the catalyst (OH^-) is regenerated. Ketones condense similarly.

Aldols (aldehyde-alcohols) are stable and may be isolated. They, however, can be dehydrated easily by heating the basic reaction mixture or by a separate acid-catalyzed reaction. Thus if the above reaction mixture is heated, the product is dehydrated to crotonaldehyde (2-butenal).

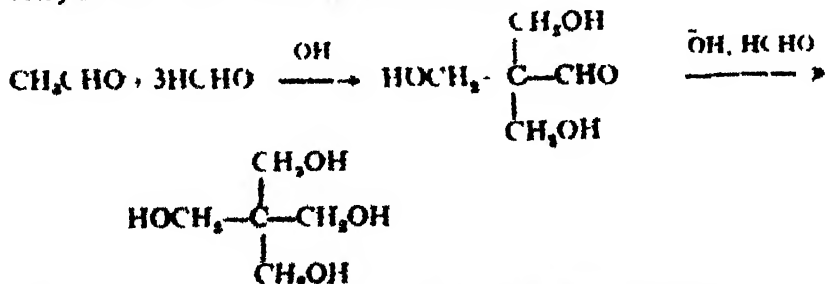


An aldol condensation can also take place between an aldehyde and ketone, as well as between two ketone molecules.



For ketones, however, the reaction is much less favorable. With acetone only a few per cent of the addition product diacetone alcohol is present at equilibrium. This is understandable on the basis of steric hindrance. Acetone forms an enolate ion but is poor in accepting the anion formed. Therefore, in contrast the addition of acetone to formaldehyde occurs readily. Formaldehyde cannot form an enolate ion because it has no α -hydrogen atom but it can easily accept the enolate ion as it is free from steric and electronic factors. Indeed, all the six α -hydrogens in acetone can be easily replaced by $-\text{C}(\text{H}_2)\text{OH}$ groups.

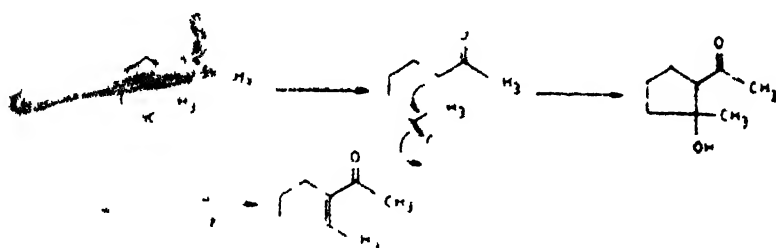
The aldol reaction between acetaldehyde and formaldehyde is rather rapid and is of commercial importance. In the presence of calcium hydroxide, addition occurs three times and leads to trihydroxymethylene acetaldehyde (which has no α -hydrogen) undergoes a crossed cannizzaro reaction with formaldehyde to give a tetrahydroxy alcohol known as pentaerythritol. This is illustrated as follows.



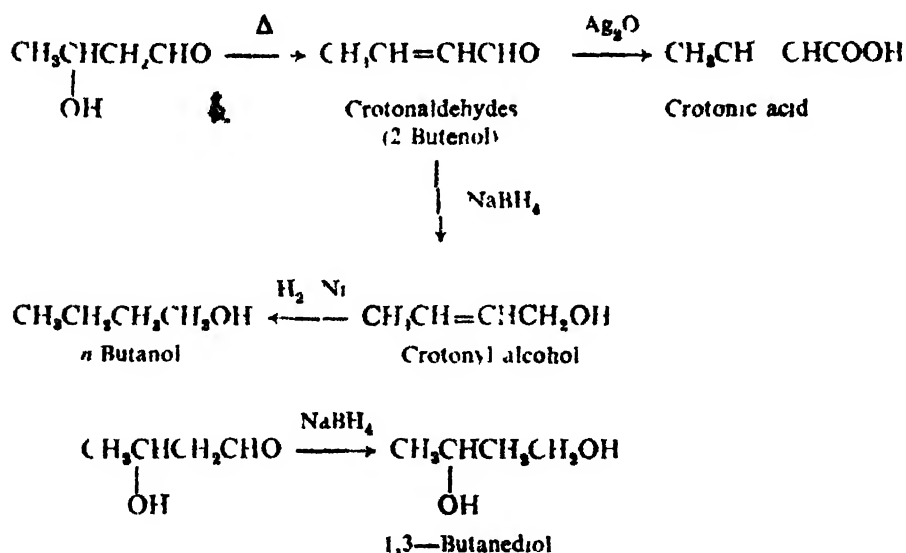
This alcohol is used in the preparation of surface coatings.

The reaction between acetaldehyde and acetone is inefficient because of the faster self-condensation of the former component

An intramolecular aldol condensation occurs more readily than the intermolecular one. This is exemplified as follows

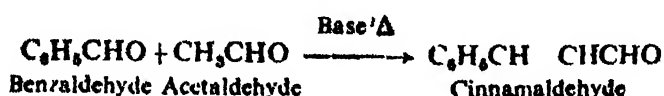


The aldol condensation product contains two functional groups, therefore, a number of subsequent reactions can be carried out to obtain important derivatives.

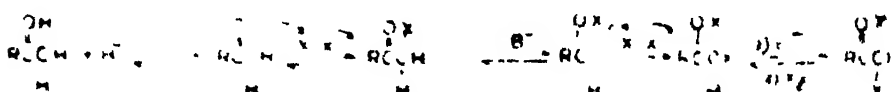


Mixed Aldol Condensation An aldol condensation between two different aldehydes containing an α -H each gives a mixture of four products and is called *mixed* or *crossed* aldol condensation. It is generally difficult to separate such a mixture. A mixed aldol condensation yielding a pure product can, however, be accomplished under two conditions (1) One of the reactants does not have an α -H and thus cannot enolize, such as an aromatic aldehyde or formaldehyde, and (2) the second carbonyl compound which possesses an α -H, is added slowly to a mixture of the first reactant and base so that it is mainly the enolate of the first carbonyl compound that is the

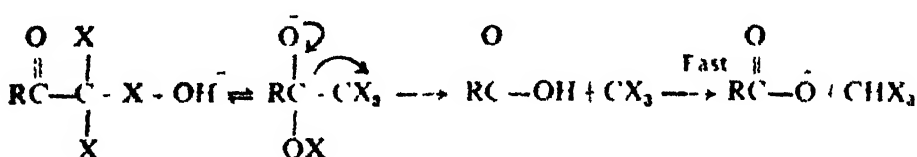
nucleophile. For example, the condensation of benzaldehyde with acetaldehyde proceeds smoothly to give cinnamaldehyde.



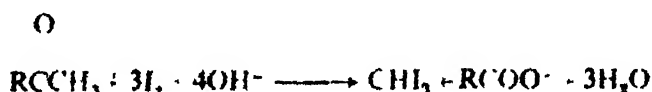
6. *The Haloform Reaction:* Methyl ketones react with halogens in the presence of base to yield a trihaloketone according to the following steps:



The trihalo ketone is not isolated but reacts further with hydroxide ion to give carboxylate ion and a corresponding trihalomethane (i.e. a haloform). The overall reaction is known as the *haloform reaction*.

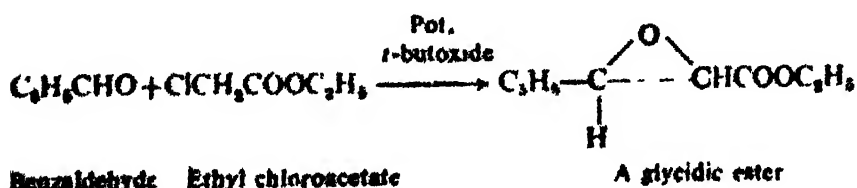


The reaction of a ketone with iodine and sodium hydroxide is called the *iodoform reaction*.



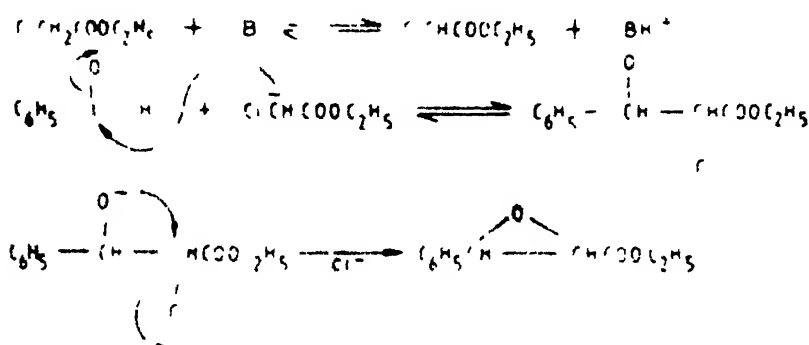
This reaction is used in structure determination as compounds containing the $-\text{CHOHCH}_3$ group give a positive iodoform test. Thus even ethyl alcohol and acetaldehyde give positive iodoform test.

7. *The Darzens Condensation:* In this reaction a halogenomethylene compound, in the presence of a base, reacts with an aldehyde or ketone to yield an α, β-epoxy ester called a *glycidic ester*. Benzaldehyde, on condensation with α-chloroacetate, in the presence of sod. ethoxide yields ethyl β-phenylglycidate.

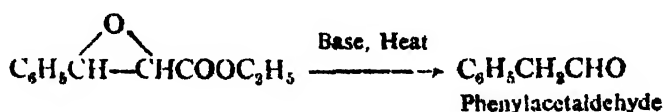


Both aromatic aldehydes and ketones give good yields in this reaction but aliphatic aldehydes give poor yields, presumably they form aldol products. Aldehydes also react faster than ketones.

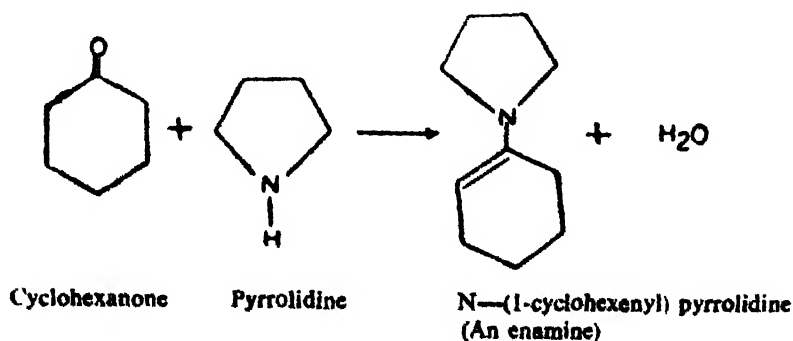
A number of base-solvent systems have been employed but pot *t*-butoxide *t*-butanol has proved to be the most suitable. The Darzens condensation is carried out under nitrogen atmosphere and with the exclusion of moisture. An essential requirement for this reaction is that the halogenomethylene compound should contain an α -hydrogen. The mechanism of the reaction proceeds through an enolate ion and is formulated below:

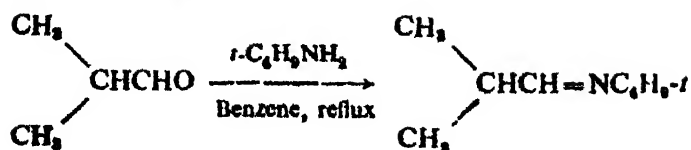


The first two steps are similar to the aldol condensation. In the last step an intramolecular S_N2 attack takes place with the closure of the epoxide ring. The hydrolysis and decarboxylation of glycidic esters provides a means for the homologation of aldehydes and ketones.

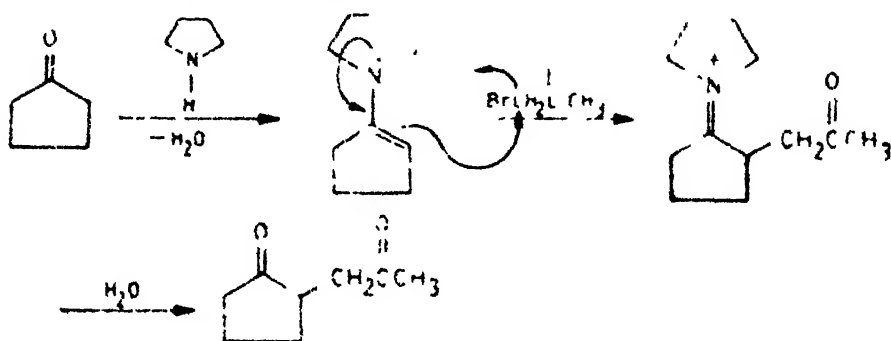


8. *Enamine Formation*: Aldehydes and ketones react with secondary amines to form *enamines* (ene+amines).

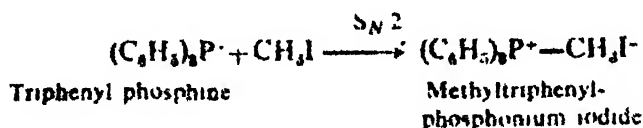




Enamines can be alkylated using α -haloketones, halo esters, primary or benzyl halides as alkylating agents.



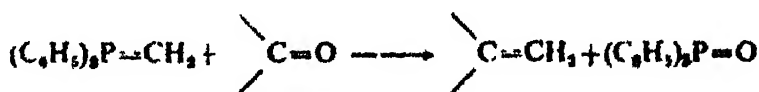
9. *The Wittig Reaction* Trialkyl- or triphenyl-phosphorus compounds (phosphines) can be alkylated by nucleophilic displacement of an alkyl-halide



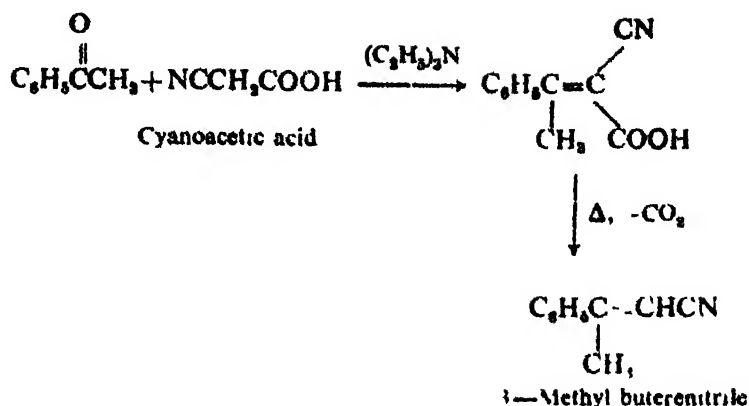
These quaternary phosphonium salts react with strong bases to form *vinyl* ionic intermediates called *ylides*. Phosphorus ylides are generally stable although highly reactive



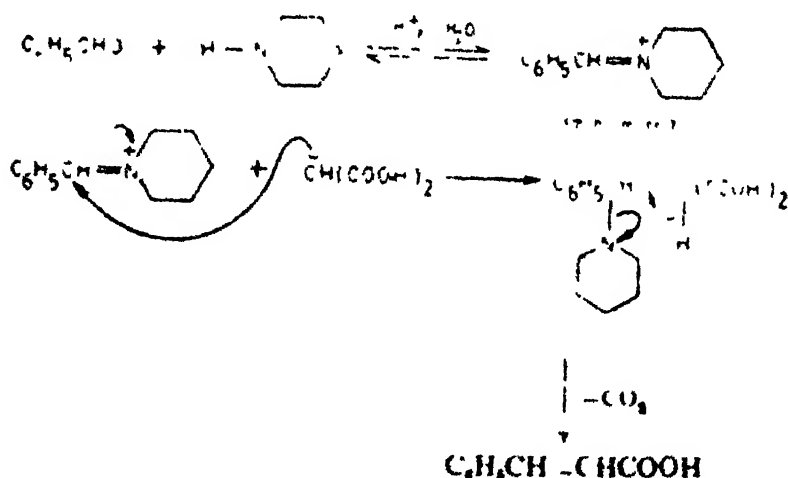
Ylides are strong nucleophiles and can condense with an aldehyde or ketone with the resultant formation of an olefin.



This reaction thus provides a versatile means for the synthesis of alkenes, as illustrated for the formation of methylenecyclohexane.

**Mechanism**

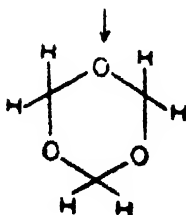
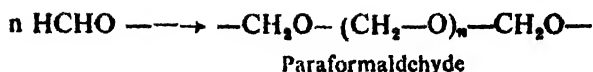
The Knoevenagel condensation requires the presence of a catalytic amount of an acid in addition to the base. Therefore, intermediate formation of an imine or iminium salt is involved and the mechanism may thus be formulated in the following steps.



The iminium salt reacts with the enolate ion of the ester to produce an intermediate amino compound. This eliminates the amine to form the unsaturated product which on decarboxylation yields cinnamic acid.

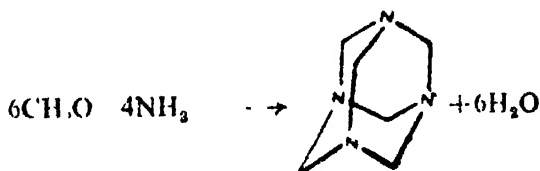
17.4.1 Reactions Given by Aldehydes Only

1 **Trimerization of Aldehydes:** Formaldehyde is readily available in solution but evaporation of a formaldehyde solution results in a solid which is a mixture of the linear polymer, paraformaldehyde and the cyclic trimer trioxane. On heating both decompose to give back formaldehyde.



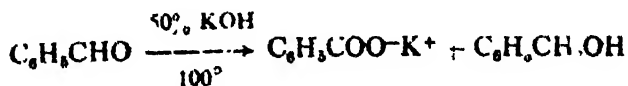
Trioxane

2 *Reaction with Ammonia* With ammonia, formaldehyde produces a tricyclic compound, hexamethylenetetramine ($\text{C}_6\text{H}_{12}\text{N}_4$) also known as *urotropine*,



Urotropine

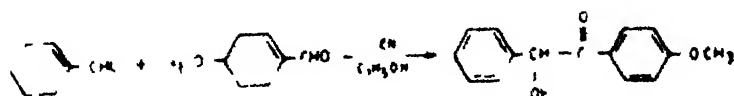
3 *The Cannizzaro Reaction:* An aliphatic or aromatic aldehyde possessing no α -hydrogen atom when treated with a conc. solution of sodium hydroxide undergoes an oxidation reduction reaction. One half of the aldehyde is reduced to a primary alcohol and the other half is oxidized to a carboxylic acid.



Mechanism

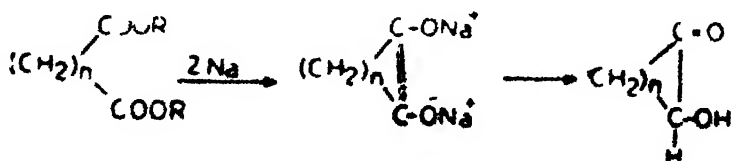
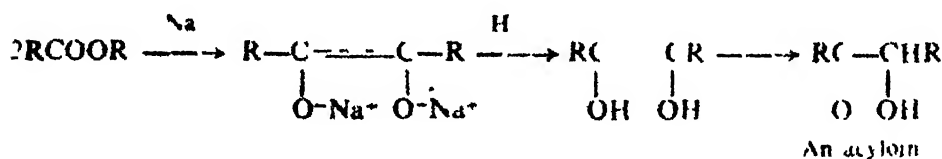
The hydroxide ion adds to the carbonyl carbon atom as the first step. The oxyanion loses a hydride ion (H^-) which is transferred to another molecule of aldehyde. The H^- transfer step is very slow and difficult. This reaction therefore does not serve as a good synthetic method.

adequately acidic and can be removed by a base. The resulting carbanion then adds to another molecule of aldehyde and benzoin is obtained as shown. The benzoin condensation is largely influenced by the presence of electron-donating groups on the aromatic nucleus. Electron-donating effect of the substituent makes the carbonyl carbon atom less electrophilic and thus less susceptible to attack by the cyanide ion. Benzoin from mixed ketones can also be obtained.

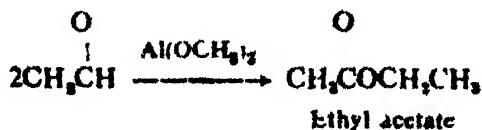


4-Methoxybenzoin

An α -hydroxyketone is called a benzoin. It can be oxidized with Benedict's reagent and also forms hydrazone with hydrazine. β -Hydroxy ketones, such as benzoin, belong to a class of compounds known as acyloins. Aliphatic, as well as cyclic acyloins, can be obtained by a bimolecular reduction of mono- and di-esters respectively, which is analogous to the reduction of ketones to pinacols. The formation of acyloins is called *acyloin condensation*. This reaction is useful in the synthesis of large ring compounds.

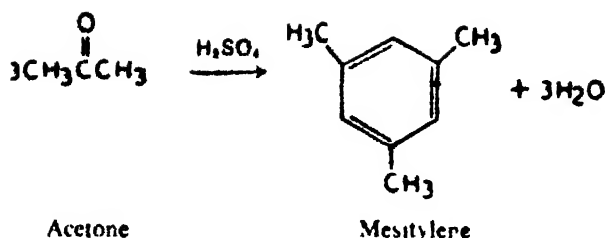


6. Tishcheiko Reaction Two molecules of an aliphatic aldehydes in the presence of an alkoxide form a molecule of ester.

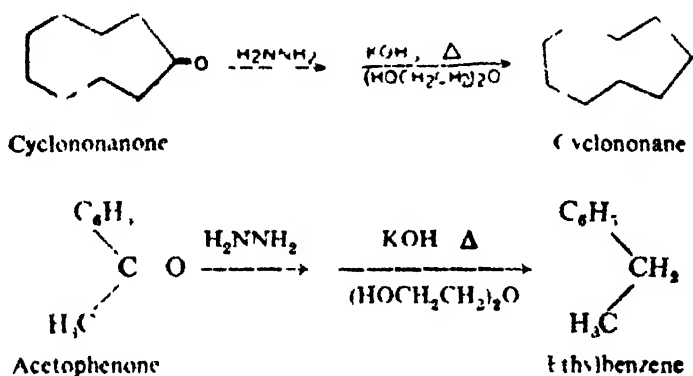


17.4.2 Reactions Given by Ketones Only

1. Ketones, in the presence of sulfuric acid, lose a molecule of water and form a cyclic product.

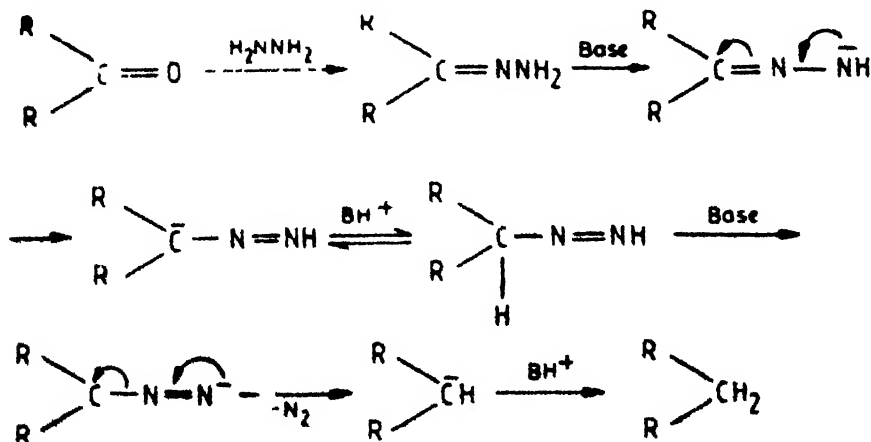


2. The Wolff-Kishner Reduction: Although the reduction of a carbonyl group leads to an alcohol, certain special methods can be used to convert it into the methylene group. This reduction is a useful reaction for the direct conversion of a carbonyl to a methylene group on heating the hydrazone of the ketone with NaOH



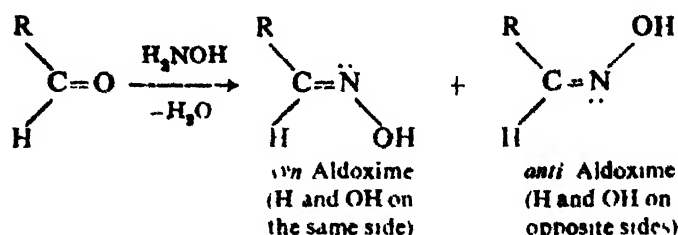
Mechanism

The procedure consists of the conversion of a ketone to a hydrazone on treatment with hydrazine. This hydrazone loses a proton to the base to form an anionic intermediate which is in equilibrium with a double bond

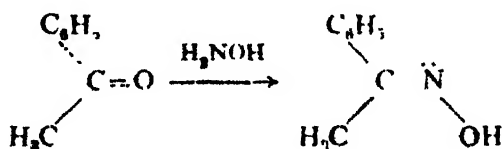


isomer. The latter picks up a proton and the intermediate expels nitrogen to form a carbanion. This being unstable picks up a proton from the solvent to form a hydrocarbon.

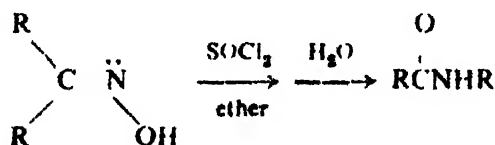
3. *The Beckmann Rearrangement*: Both aldehydes and ketones react with hydroxylamine to form aldoximes and ketoximes respectively. Since there is no free rotation about the carbon—nitrogen double bond, two geometric isomers are thus possible.



Since such a relationship is not easily determined for ketoximes, they cannot be distinguished in the same manner.

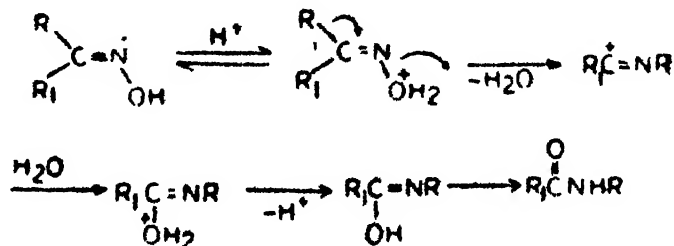


These oximes are transformed into amides on treatment with strong acids (PCl_5 , H_2SO_4 , SOCl_2 , PPA, etc.).



Mechanism

The mechanism of the Beckmann rearrangement involves the shift of an alkyl (or aryl) group from carbon to electron deficient nitrogen from the protonated oxime.



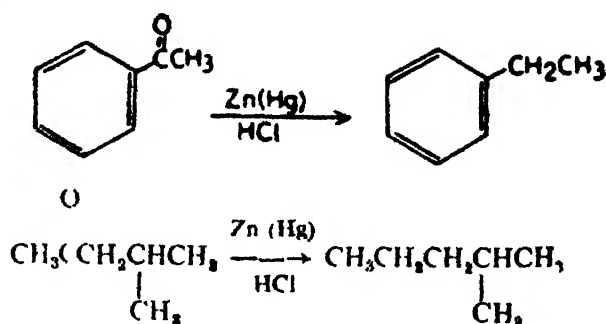
The cation so formed after the migration of the group reacts with water to give the enol form of an amide which tautomerizes to an amide.

This reaction is stereospecific because the alkyl (or aryl) group *anti* (*trans*) to the oxime hydroxyl group migrates preferentially.

The Beckmann rearrangement can also be promoted photochemically. In this case the reaction proceeds through an oxaziridone (a three-membered ring with an oxygen and nitrogen) intermediate.

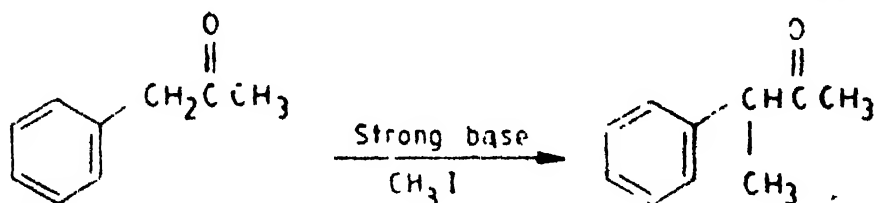
An important application of this reaction is the formation of caprolactam from cyclohexane oxime which is employed in the manufacture of Nylon-6 polymer.

4. *The Clemmensen Reduction*: This is a method to carry out the reduction of a ketone directly to the methylene group. It involves the refluxing of a ketone with amalgamated zinc and hydrochloric acid. The zinc and mercury metals combine in non-stoichiometric proportions to give the reduced product.



This method is unsatisfactory for aldehydes as they give a mixture of products.

5. *Alkylation at the α -Carbon Atom*: Ketones, in contrast to aldehydes, can be alkylated at the α carbon atom via the formation of an enolate ion.

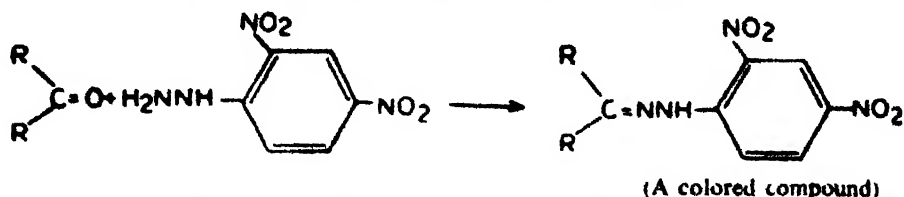


This reaction requires the presence of a strong base. Sodium methoxide or ethoxide cannot be used as they convert the ketone into an enolate anion only partially and thus aldol condensation product is formed. Stronger bases such as pot. *t*-butoxide, sodium hydride or sodium amide are capable of converting the ketone quantitatively to the enolate anion and are thus preferred, side products such as di- and tri-alkylated products are also formed in this reaction.

17.5 DISTINCTION BETWEEN ALDEHYDES AND KETONES

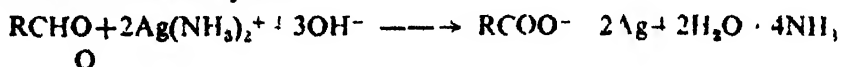
Aldehydes and ketones having less than five carbon atoms are soluble in water just like alcohols. Moreover, like alcohols, they are also neutral. It

is, therefore, necessary first to distinguish them from alcohols. One useful method is to treat the unknown with a freshly prepared solution of 2, 4-dinitrophenylhydrazine. This reagent reacts with a large number of carbonyl compounds to form colored solid derivatives which have sharp melting points. Alcohols, however, fail to react with this reagent.



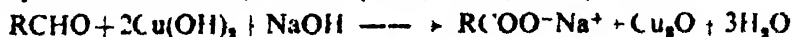
To distinguish an aldehyde from a ketone, advantage is taken of the ease with which an aldehyde is oxidized to carboxylic acid. Three reagents, namely Tollens', Fehling's and Benedict's solutions are commonly employed for this purpose.

Tollens' reagent is an ammoniacal solution of a silver ion-ammonia complex. It is readily reduced to metallic silver by easily oxidizable compounds such as aldehydes.



A silver mirror is deposited along the sides of the glass tube. This process is actually used in the manufacture of mirrors, with formaldehyde serving as an inexpensive aldehyde.

Fehling's solution contains cupric ions in aqueous sodium hydroxide. Aldehydes reduce the cupric ions (Cu^{2+}) to cuprous (Cu^+) ions.



A red precipitate of cuprous oxide separates out.

Benedict's solution is similar to the Fehling's solution except that cupric ions are complexed with citric acid.

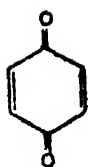
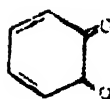


The latter two reagents are weak oxidizing agents. They oxidize aliphatic aldehydes but are not capable of oxidizing the aromatic aldehydes such as benzaldehyde.

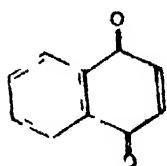
A specific test for aldehydes is the restoration of the pink color of Schiff's reagent. A *Schiff's reagent* is prepared by passing SO_2 gas through a solution of a pink colored dye-*fuchsin* and a colorless solution is obtained. Aldehydes restore the pink color while ketones do not.

17.6 QUINONES

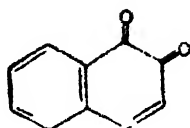
A quinone is a compound with two carbonyl groups and two double bonds in a six-membered ring. The carbonyl group may be present in the 1, 4—or 1, 2—positions.

*p*-Benzoquinone*o*-Benzoquinone

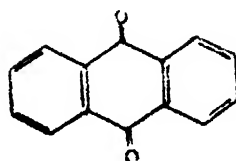
Quinones are also derived from other aromatic hydrocarbons, some examples are given below



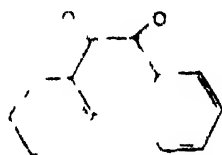
1,4-Naphthaquinone



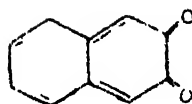
1,2-Naphthaquinone



9,10-Anthraquinone



9,10-Phenanthraquinone

2,3-Naphthaquinone
(unstable)

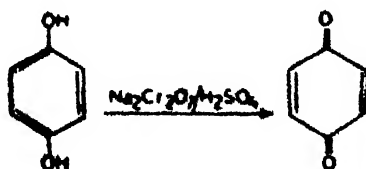
17.7 PHYSICAL PROPERTIES OF QUINONES

Quinones occur in plants, lichens, marine organisms and fungi and many of them are responsible for the red, orange and yellow colors found in plants and animals. They also take part in oxidation reduction cycles essential to the living organisms.

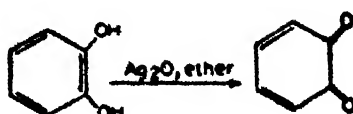
17.8 PREPARATION OF QUINONES

Quinones may be prepared by the following oxidation methods.

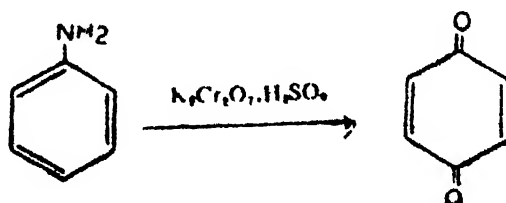
1. *p*-Benzoquinone is obtained by the oxidation of hydroquinone.



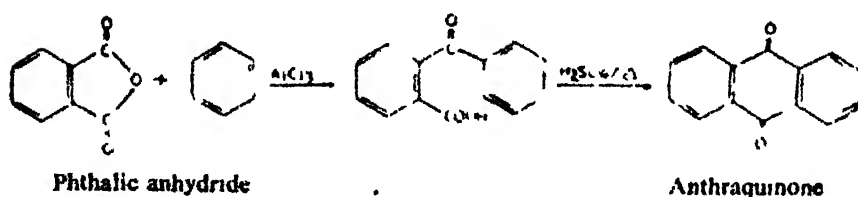
o-Benzoquinone is obtained by the oxidation of catechol.



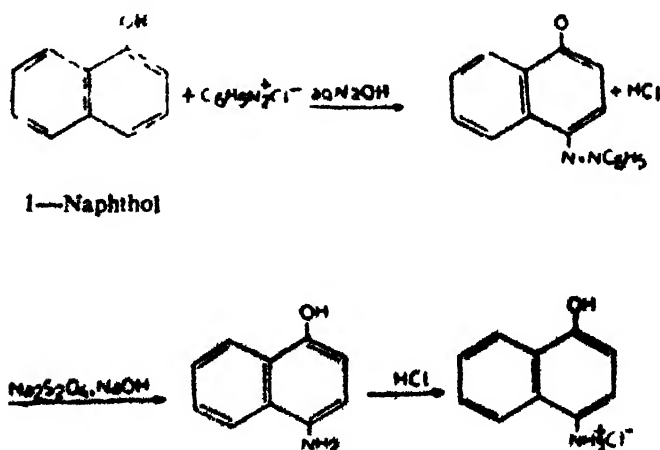
Quinones may also be prepared by the oxidation of *o*- or *p*-aminophenols and in many cases by the direct oxidation of phenol or aniline.

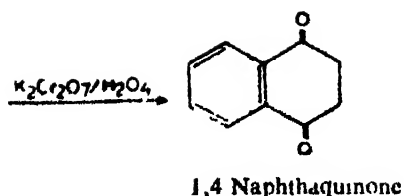


2 Anthraquinone is obtained in the following manner



3. The following sequence of reactions may be employed to prepare 1,4-naphthaquinone starting from 1-naphthol.

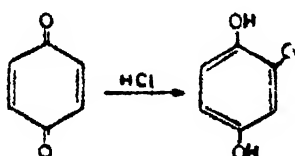




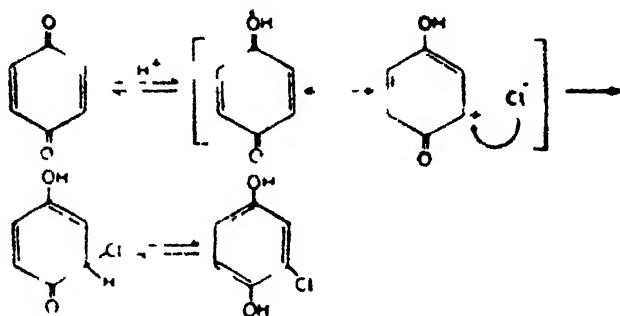
17.9 REACTIONS OF QUINONES

Quinones are not aromatic compounds, instead they are α, β -unsaturated carbonyl compounds and display reactions typical of such structures.

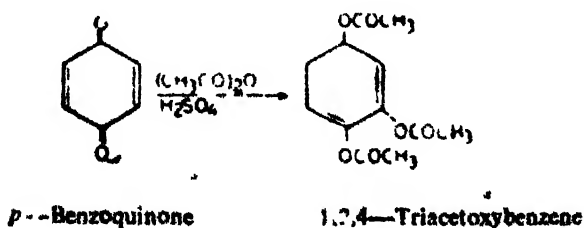
1. *Addition of HCl*: Hydrochloric acid adds to yields *o*-chlorohydroquinone

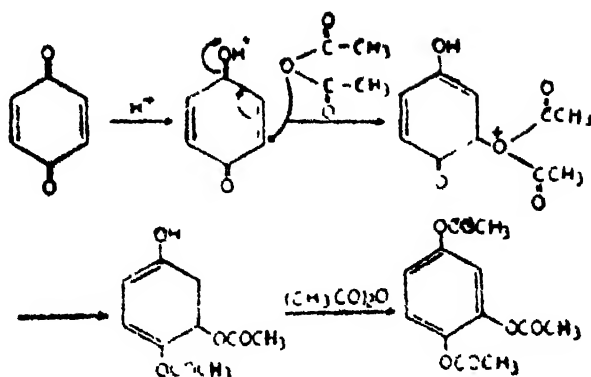


Mechanism

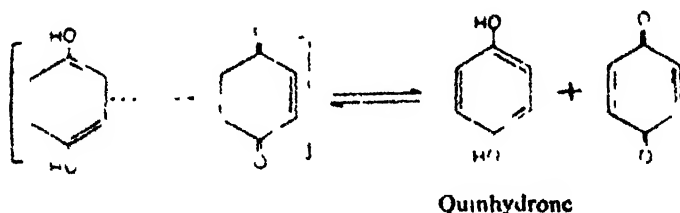


2. Acid-catalyzed addition of acetic anhydride to *p*-benzoquinone leads to 1,2,4-triacetoxybenzene.

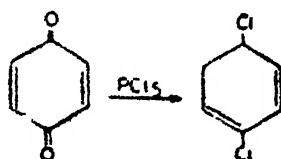


Mechanism

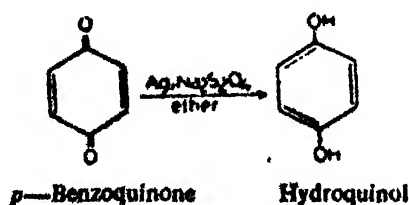
3. An equimolar mixture of *p*-benzoquinone and hydroquinone forms a dark green colored complex of a donor-acceptor type (in which one molecule donates electrons while the second accepts) called quinhydrone



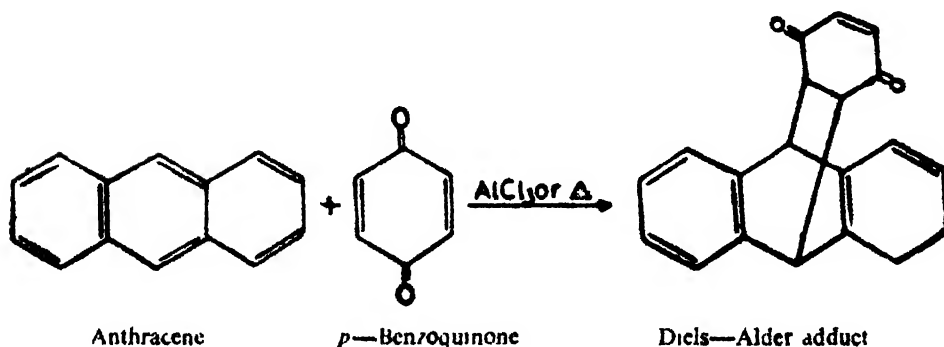
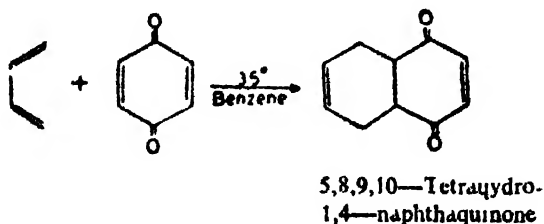
4. *p*-Dichlorobenzene is obtained by the replacement of oxygen in *p*-benzoquinone with chlorine using PCl_5 ,



5. **Reduction:** Since these compounds are cyclic diketones, they are converted to hydroquinones



6. **Diels-Alder[†] Reaction:** *p*-Benzoquinone functions as a dienophile and forms Diels—Alder adducts with several types of dienes.



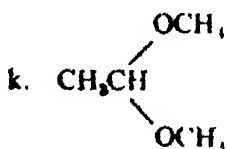
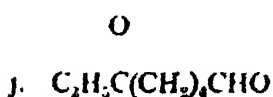
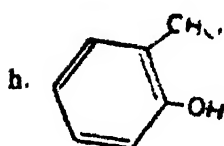
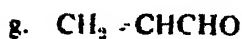
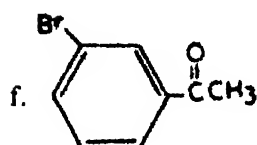
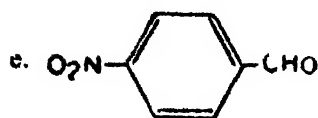
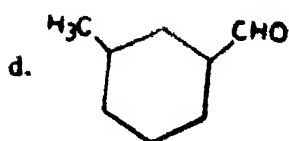
17.10 USES OF QUINONES

Hydroquinone is used as a photographic developer. Quinhydrone is employed in the measurement of H⁺-ion concentration potentiometrically. Quinones, in general, are also used in medicines.

QUESTIONS

17.1 Suggest names for the following structures:

- O
- a. $\text{CH}_3\text{CCH}_2\text{CH}_3$
- b. $\begin{array}{c} \text{CH}_3 \\ \diagdown \\ \text{CHCH}_2\text{CH}_2\text{CHO} \\ \diagup \\ \text{CH}_3 \end{array}$
- c.

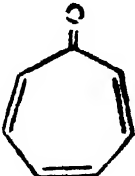


17.2 Postulate a suitable mechanism for each of the following reactions:

- The Beckmann rearrangement
- The Perkin reaction
- The Benzoin condensation
- The Aldol condensation
- The Darzens condensation
- The Wittig reaction

17.3 Offer explanation for the following observations:

- Benzaldehyde does not undergo aldol condensation.
- Chloral hydrate is stable.
- Boiling points of butanal (76°) and 1-butanol (118°) are very different but their solubility in water is quite similar.
- 2,4-Pentanedione is highly acidic.

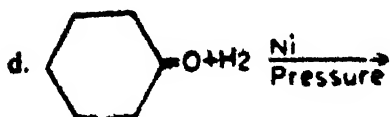
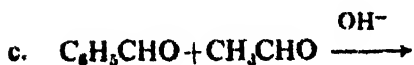
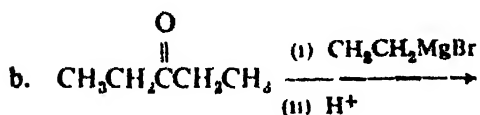
e The ketone tropone  is very basic in character and

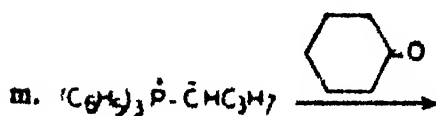
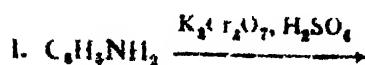
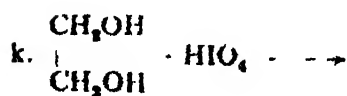
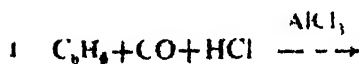
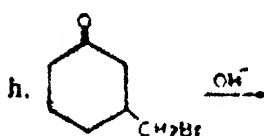
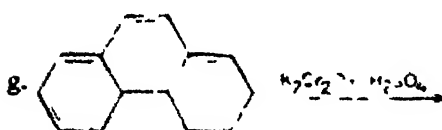
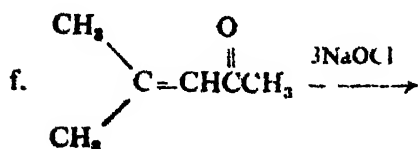
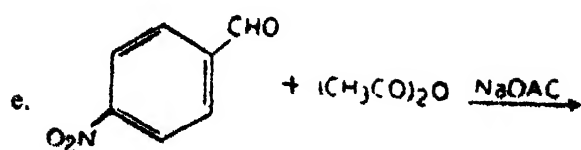
forms stable salts with HCl

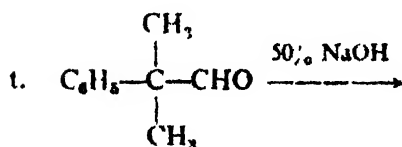
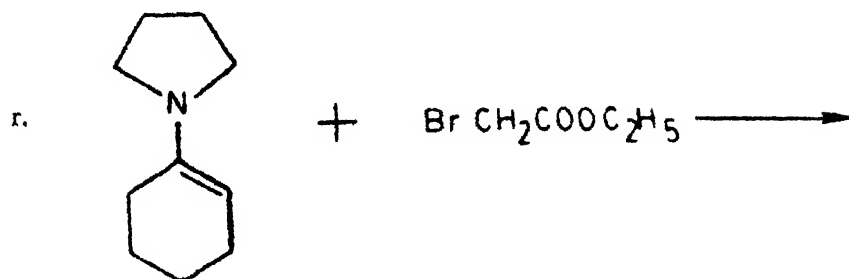
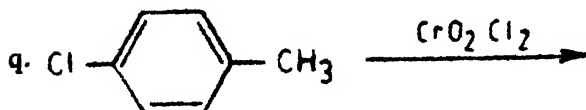
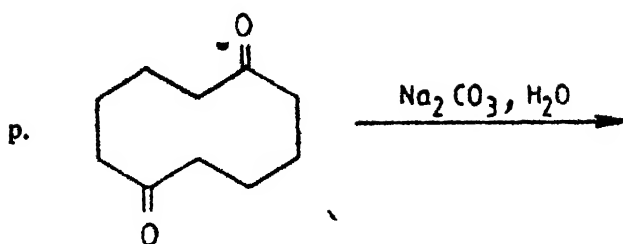
- Wolff-Kishner reduction of ketones is preferred over the Clemmensen reduction.
- Hydroxylamine is employed in the form of its hydrochloride salt.
- Benzaldehyde reacts faster than *p*-methoxybenzaldehyde with HCN.
- Acetophenone but not benzophenone forms an adduct with NaHSO_3 .

17.4 Explain why only the α -hydrogen atom in aldehydes and ketones is involved in the aldol condensation.

17.5 Predict products of the following reactions.







7.6 Which of the following compounds would give a positive iodoform test ?

- 2-Butanol
- 1-Pentanol
- Acetone
- 3-Pentanone

- e. 2—Pentanone
 - f. 3—Pentanol
 - g. 1—Phenylethanol
 - h. Acetophenone
- 17.7 Give one example each of Clemmensen and Wolff-Kishner reductions.
- 17.8 State the reactions which differentiate aliphatic from aromatic aldehydes.
- 17.9 A liquid of the molecular formula, C_7H_8O , forms an oxime, reduces Fehling's solution and undergoes the Cannizzaro reaction. What structural formula would you assign to this liquid?
- 17.10 An ether solution of acetophenone reacts with bromine in the presence of traces of $AlCl_3$ to give $C_6H_5COCH_2Br$ in good yield. If 2.5 molar equivalents of $AlCl_3$ are mixed with acetophenone immediately before addition of bromine, the mixture reacts slowly to give *m*-bromoacetophenone. Suggest a reason for this change.
- 17.11 Arrange the following compounds in order of increasing reactivity towards the addition of HCN.
Acetone, acetaldehyde, methyl *t*-butyl ketone and di *t*-butyl ketone
- 17.12 Suggest tests that will distinguish the following pairs of compounds.
- a. Acetic acid and propanal
 - b. Acetaldehyde and acetone
 - c. Acetaldehyde and propanal
 - d. 4—Pentyn—2—one and 3—pentyn—2—one
 - e. Acetone and *iso* propanol.
 - f. 1-Bromo-2-butanone and 4-bromo-2-butanone
 - g. 2—Pentanone and 3—pentanone
- 17.13 Explain why HCN will add to the double bond in $CH_2=CHCOO^-$ but not in $RCH=CHR$.
- 17.14 a. What are the reactions associated with the names of Perkin and Cannizzaro?
b. How would you prepare acetophenone from benzene?
- 17.15 a. Give any four methods for the preparation of alkanones.
b. Describe mechanism of addition reaction of alkanones selecting at least two examples
- 17.16 Describe the properties of acetophenone. How can you obtain the following from it
- a. Benzoic acid
 - b. Phenacyl bromide
 - c. Benzoyl acetone

- 17.17 What are quinones? Describe two methods for the preparation of *o*-benzoquinone and *p*-benzoquinone. Describe their important physical and chemical properties.
- 17.18 Compare and contrast the properties of acetaldehyde and acetone. Give equations of three reactions.
- 17.19 Outline the different methods for preparing benzaldehyde. Describe its important properties.
- 17.20 Describe the important methods for preparing benzaldehyde on a large scale. In what reactions does it differ from benzophenone?
- 17.21 a Describe five nucleophilic addition reactions of a carbonyl group
 b How would you convert acetaldehyde into acetone, diethyl ether and aldol?
- 17.22 a How are ketones prepared from
 (i) Acids
 (ii) Acid derivatives
 b. How does an aldehyde react with
 (i) Hydrocyanic acid
 (ii) Ammonia
 (iii) Thioalcohols
- 17.23 Compound A, having the empirical formula C_7H_8 , is chlorinated in sunlight to give a product which is hydrolyzed to produce B. B, after oxidation reacts with acetic anhydride in the Perkin reaction to produce an acid C, which has an equivalent weight of 148. Give the names and structures of A, B and C.

Carboxylic Acids

Organic compounds which contain a carboxyl group, $\begin{array}{c} \text{O} \\ \parallel \\ \text{—C} \\ | \\ \text{OH} \end{array}$ (the name is

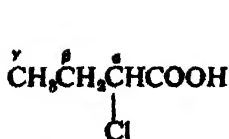
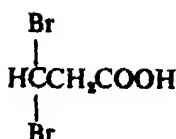
derived by linking carbonyl and hydroxyl groups) are termed as carboxylic acids. The carbonyl group changes the properties of the —OH group and *vice versa*. The carbon atom in a carboxylic acid is present in its highest oxidation state which makes it stable toward further oxidation. For this reason, acids occur abundantly in natural products such as oils, fats, amino acids, proteins. The carboxylic acids ionize in water to form a carboxylate ion and hydronium (H_3O^+) ion.

Section A: ALIPHATIC CARBOXYLIC ACIDS

Aliphatic carboxylic acids may be considered as derivatives of the corresponding alkanes, in which one H-atom has been replaced by —COOH function, for instance, CH_4 , (Methane) to CH_3COOH , (Acetic acid). They possess the general molecular formula $\text{C}_n\text{H}_{2n+1}\text{COOH}$. Acids containing one, two or three carboxylic functions are referred to as *mono-*, *di-*, and *tri-*carboxylic acids. Carboxylic acids may be *aliphatic* or *aromatic*. The former type may further be sub-divided into *saturated*, *unsaturated*, *hydroxy* and *halo-carboxylic acids*. These are weak acids and their ionization in water is far from complete.

18.1 NOMENCLATURE OF CARBOXYLIC ACIDS

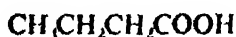
The common name of carboxylic acids is based on its source or origin in nature, for example, formic acid (Latin, *formica*), acetic acid (Latin, *acetum*, vinegar) butyric acid (*butyrum*, butter), etc. The position of a substituent present on the chain is specified by the Greek alphabet α , β , γ and so on. The carbon atom next to the carboxyl group is considered as α .

 α -Chlorobutyric acid β, β -Dibromopropionic acid

The systematic name is derived from the name of the corresponding alkane by dropping the ending *-e* and putting the suffix *-oic acid*.

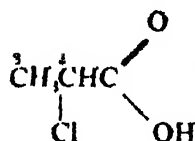
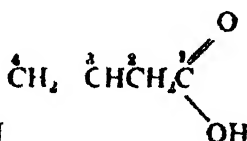
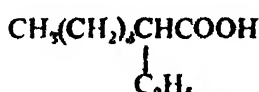


Methanoic acid

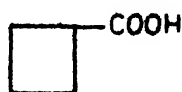


Butanoic acid

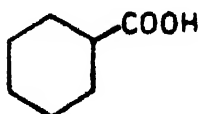
The position of the substituent is indicated by the usual numerals

 γ -Chloropropionic acid γ -Butyric acid γ -Ethylhexanoic acid

The cyclic acids cannot be named in this manner. To name them the name of the corresponding cycloalkane precedes the word carboxylic acid.



Cyclobutanecarboxylic acid

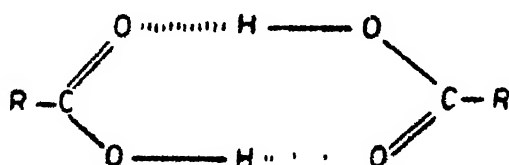


Cyclohexanecarboxylic acid

18.2 PHYSICAL PROPERTIES OF ALIPHATIC CARBOXYLIC ACIDS

The lower molecular-weight aliphatic acids (C_1 - C_{10}) are colorless liquids with sharp odor-methanoic, ethanoic and propanoic acids have vinegar like odors, while acids from C_4 - C_{10} have distinguishing goat-like odors. Higher acids are practically odorless. Butyric acid is responsible for the unpalatable taste of rancid butter. It is also present in human sweat. Higher fatty acids are wax-like solids. The salicylic acids are, however, crystalline

solids. Carboxylic acids, as a class, have higher boiling points than alcohols. Propionic acid (b.p. 141°) boils 44° degree higher than the alcohol of comparable molecular weight, *n*-propyl alcohol (b.p. 97°). This is due to the presence of intermolecular hydrogen-bonding which gives a dimeric character to the acids. The molecules of carboxylic acids are attracted by hydrogen-bonding to a larger extent because of the presence of two polar groups, in case of acids (the carbonyl and the hydroxyl groups) as compared to only hydroxyl group in case of alcohols.

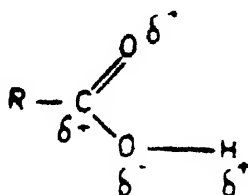


This causes dimerization of the acid and reduces the vapor pressure and increases the boiling point to a large extent than would be expected from the molecular weight of the monomeric acid itself

Table 18.1 Physical Constants of Carboxylic Acids

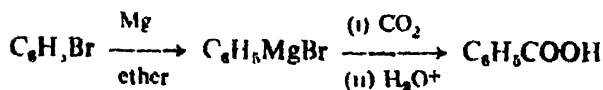
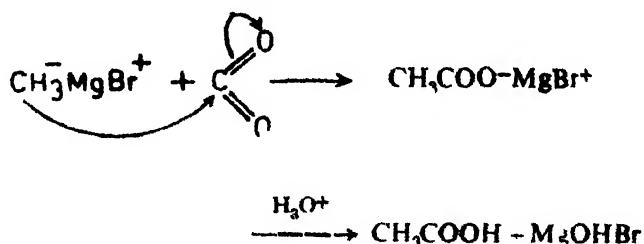
Acid	Formula	m p ($^{\circ}\text{C}$)	b p ($^{\circ}\text{C}$)
Formic acid	HCOOH	-	100.5
Acetic acid	CH_3COOH	16.6	118
Propionic acid	$\text{CH}_3(\text{CH}_2)\text{COOH}$	22	141
Butyric acid	$\text{CH}_3(\text{CH}_2)_2\text{COOH}$	6	164
Valeric acid	$\text{CH}_3(\text{CH}_2)_3\text{COOH}$	4	187
Caproic acid	$\text{CH}_3(\text{CH}_2)_4\text{COOH}$	-3	205
Enanthic acid	$\text{CH}_3(\text{CH}_2)_5\text{COOH}$	-8	221
Caprylic acid	$\text{CH}_3(\text{CH}_2)_6\text{COOH}$	16	239
Pelargonic acid	$\text{CH}_3(\text{CH}_2)_7\text{COOH}$	14	255
Capric acid	$\text{CH}_3(\text{CH}_2)_8\text{COOH}$	31	269
Lauric acid	$\text{CH}_3(\text{CH}_2)_{10}\text{COOH}$	44	275
Myristic acid	$\text{CH}_3(\text{CH}_2)_{12}\text{COOH}$	54	291
Palmitic acid	$\text{CH}_3(\text{CH}_2)_{14}\text{COOH}$	61	269
Stearic acid	$\text{CH}_3(\text{CH}_2)_{16}\text{COOH}$	70	287
Cyclobutanecarboxylic acid			190
Cyclopentanecarboxylic acid			212.5
Cyclohexanecarboxylic acid			232

The lower members are also miscible with water because of H—bond formation with water. The polar nature of carboxylic acids can further be recognized by the polarization of charge near the oxygen atom. They also possess appreciable dipole moments.

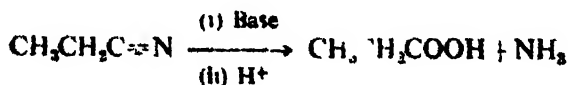


18.3 PREPARATION OF ALIPHATIC CARBOXYLIC ACIDS

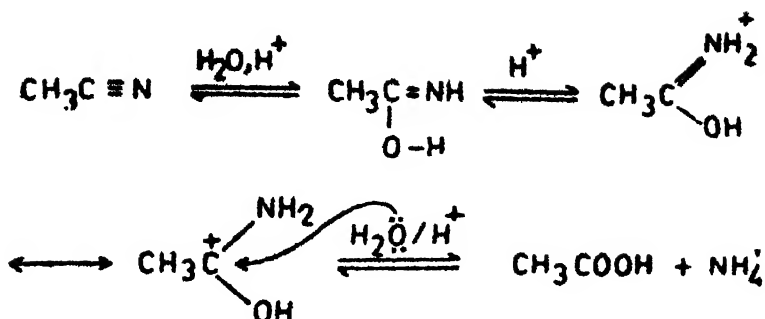
1. *From Grignard Reagents.* A Grignard reagent is treated with carbon dioxide. Dry ice is often employed as the source of carbon dioxide. The resulting complex is hydrolyzed to give an acid. The carbon atom of the carboxylic group comes from carbon dioxide.



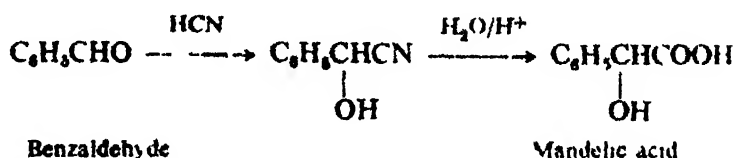
2. *Hydrolysis of Nitriles.* A highly useful method for the preparation of acids is the hydrolysis of nitriles, i.e., compounds containing a $\text{—C}\equiv\text{N}$



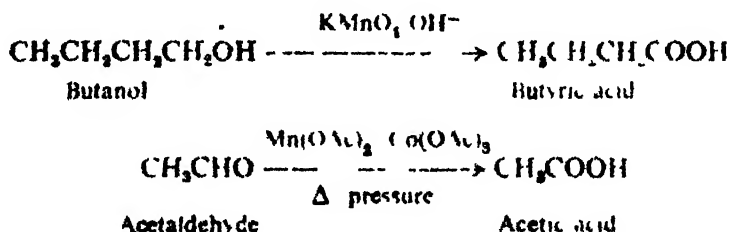
function. Hydrolysis by a base by prolonged refluxing forms the sodium salt of the acid and ammonia is liberated. The acid can be obtained by acidifying the reaction mixture. Hydrolysis can also be accomplished in acid medium.



This method is limited by the availability of a nitrile. Mandelic acid may be prepared in the following steps.

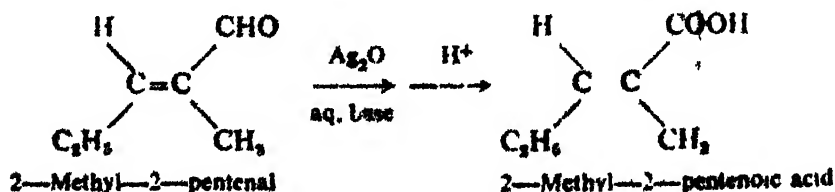


3 *Oxidation of Primary Alcohols or Aldehydes* Chemical oxidizing agents readily oxidize primary alcohols or aldehydes to carboxylic acids. The initial product of oxidation from an alcohol is an aldehyde, which is rapidly converted to the acid.

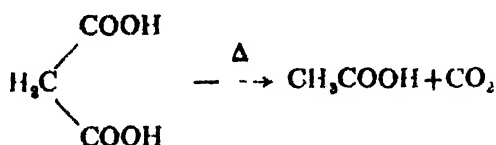


Acetaldehyde is converted by an oxidation in acetic acid over cobalt-manganese acetate as catalyst. The major fraction of the product is marked as glacial acetic acid. Acetic acid is the chief constituent of vinegar.

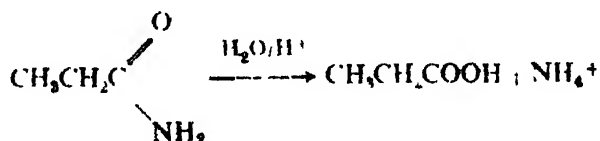
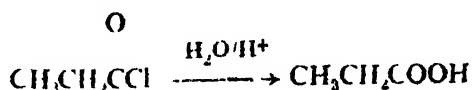
An extremely mild but selective oxidizing agent for aldehydes is silver oxide suspended in aqueous base. An unsaturated acid is obtained in good yield with this reagent because the double bond remains untouched.



4. Monocarboxylic acids may also result from the decarboxylation of dicarboxylic acids. Acetic acid is thus obtained from malonic acid.

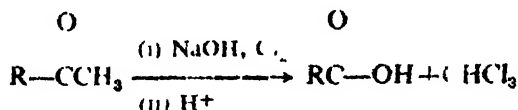


5. Another useful method constitutes the hydrolysis of carboxylic acid derivatives such as acyl halides, amides or anhydrides.



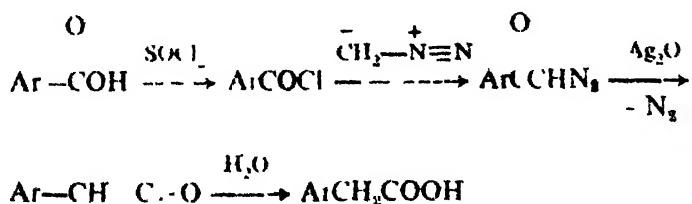
O

6. *By the Oxidation of Methyl Ketones* : Oxidation of $-\text{CCH}_3$ group with sodium hypochlorite ($\text{NaOH} + \text{Cl}_2$) results in a carboxyl group formation



It is a specific reagent for this group.

7. *Arndt-Eistert Reaction* : It is a highly useful method for preparing next higher homologue of a carboxylic acids.

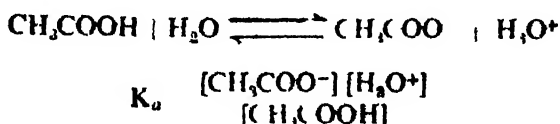


8. Formic acid may be obtained by heating carbon dioxide with an alkali. The acid is regenerated with sulfuric acid.



18.4 ACIDITY OF CARBOXYLIC ACIDS

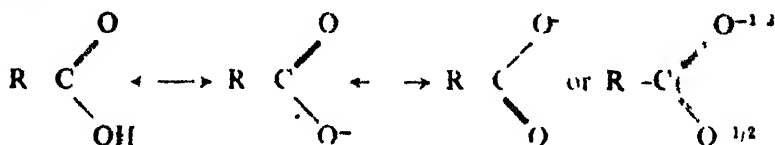
Carboxylic acids are only partially ionized in aqueous solutions and thus display weak acidic properties. A convenient way to measure the acidity of an acid is in terms of its ionization constant (K_a). For the ionization of acetic acid, the best known representative of this series, the expression for K_a is obtained as follows



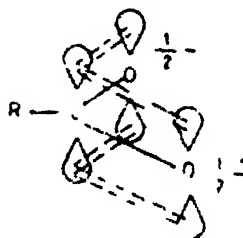
The concentration term for water is neglected since it is not affected to any appreciable extent by the ionization of the acid.

A higher value for K_a implies a strong acid. For acetic acid, K_a is 1.8×10^{-5} , a value which is observed for weak acids. The corresponding value for trichloroacetic acid (Cl_3CCOOH) is 3×10^{-1} . Thus the acidity increases by replacing the hydrogen atom with chlorine. The inductive electron-withdrawing effect augments the acidity.

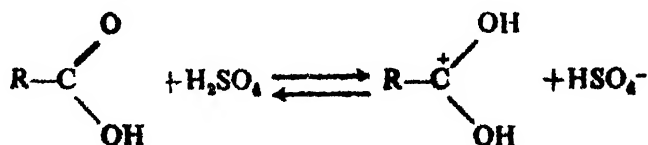
Carboxylic acids are stronger than alcohols even though they are weaker than the common mineral acids. This is so because after the carboxyl group loses a proton, the resultant carboxylate anion is stabilized by resonance.



The molecular orbital representation of the carboxylate anion is given below.



Carboxylic acids function as bases though weak ones, in the presence of strong acids. The proton is captured by the carboxylic acid and the following equilibrium is established



The contributions of conjugative and inductive effects to influence the ionization constant of carboxylic acids have been described in Chapter 3. It may be recalled that electronegative substituents have an inductive acid-strengthening effect in the case of aliphatic carboxylic acids. Electropositive groups decrease the acidity. For aromatic acids, an additional factor, i.e., the resonance of the π -electrons of the ring must be considered. The resonance stabilization of the carboxylate anion results in increased acidity of the acid.

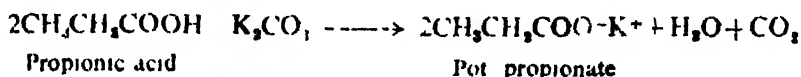
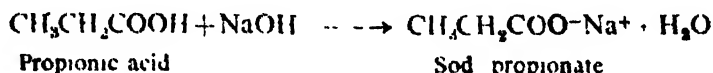
18.5 REACTIONS OF ALIPHATIC CARBOXYLIC ACIDS

The most important properties of carboxylic acids are their conversion to important functional derivatives. The reactions of carboxylic acids may be discussed under the following categories.

- (a) Reactions involving the $-\text{OH}$ group
- (b) Reactions involving the $\begin{array}{c} \diagup \\ \text{C}=\text{O} \\ \diagdown \end{array}$ group
- (c) Reactions involving the $-\text{COOH}$ group
- (d) Reactions involving the aliphatic moiety.

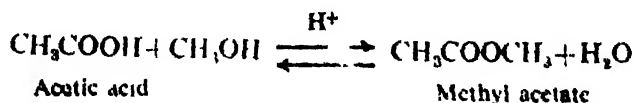
a. Reactions involving the $-\text{OH}$ group:

1. Carboxylic acids react rapidly with aqueous solutions of sod- hydroxide or pot- carbonate to form soluble salts.



Aqueous solutions of these salts are alkaline, they being salts of a strong base and a weak acid. The sodium or potassium salts of long chain fatty acids are known as soaps.

2. *Formation of Esters*: An ester may be prepared by the direct reaction between an acid and an alcohol under the catalytic effect of sulfuric acid, by a process known as *esterification*.

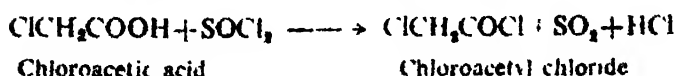
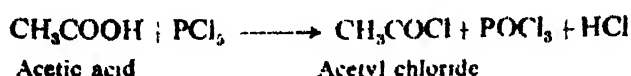


This is a reversible reaction but the equilibrium can be pushed toward the right by using an excess of the alcohol.

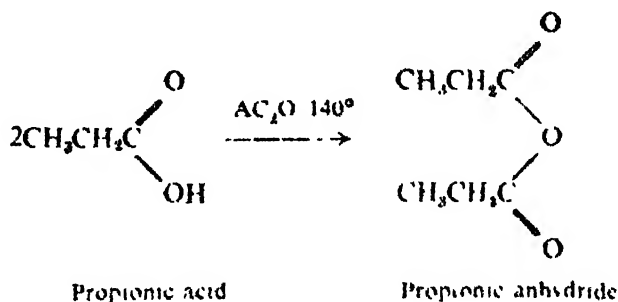
3. Amides can be prepared by treatment of the acid with aqueous ammonia in the cold. Initially an ammonium salt is formed and subsequent heating and dehydration produces an amide.



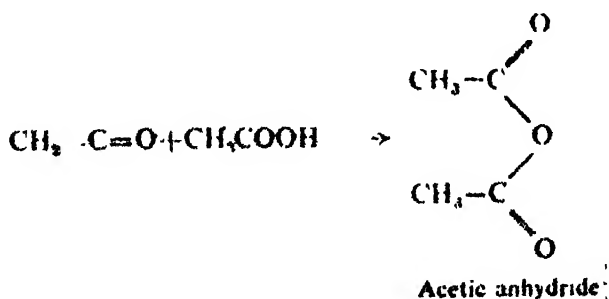
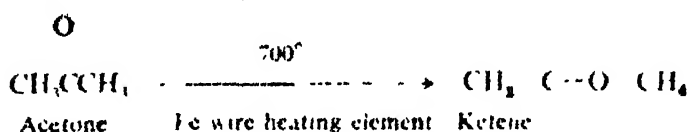
4. The acid halides may be obtained by refluxing an acid with PCl_5 or SOCl_2 . The acyl halides are obtained in good yields.



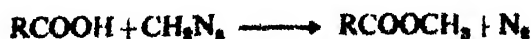
5. Symmetrical anhydrides are obtained by heating together a carboxylic acid and acetic anhydride. Acetic anhydride, however, is prepared by a



special method from ketene and acetic acid

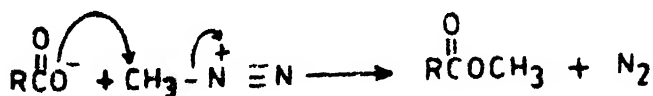
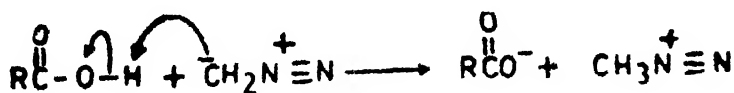


6. *Reaction with Diazomethane:* A synthetically useful reaction of carboxylic acids is the formation of methyl esters by reaction with diazomethane (CH_2N_2).



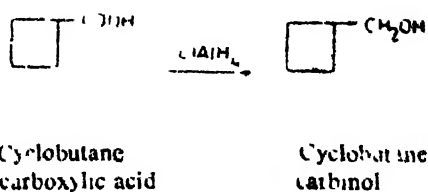
Mechanism

Initially the acid transfers its proton to diazomethane similar to acid-base reaction. The carboxylate anion then makes a nucleophilic attack on $\text{CH}_3-\text{N}^+\equiv\text{N}$, to yield the ester.

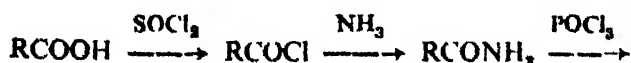


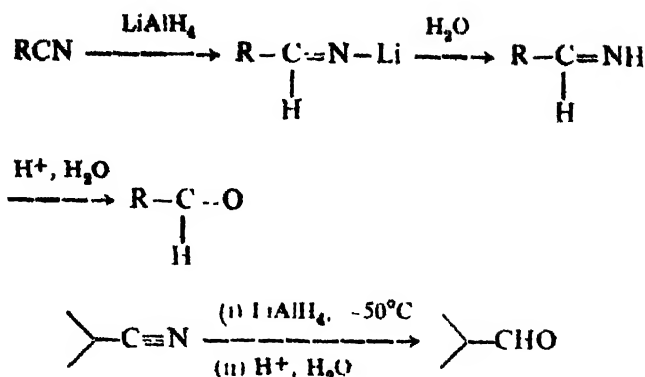
b. *Reactions Involving the Carbonyl Group:* In the carboxyl group, the carbonyl and the hydroxyl groups are in close association. This tends to modify the chemistry associated with either group alone. In particular, the type of nucleophilic addition reactions identified with the carbonyl group in aldehydes or ketones are commonly not observed with acids. This may be accounted for by the fact that an attacking base preferentially abstracts an acidic proton thus forming its carboxylate anion. The anion, in turn, because of its negative charge and large resonance energy, resists the addition of a second molecule of the attacking base. It thus does not form an oxime or phenyl hydrazone.

1 *Reduction.* Lithium aluminum hydride reduces a carboxyl group to a primary alcohol. The reduction, however, does not take place with NaBH_4 although diborane (B_2H_6) reduces it.



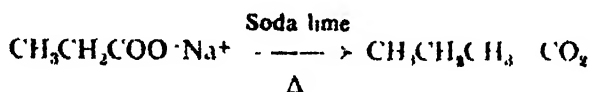
Reduction of the carboxyl group with LiAlH_4 also takes place to an aldehyde at low temperature.



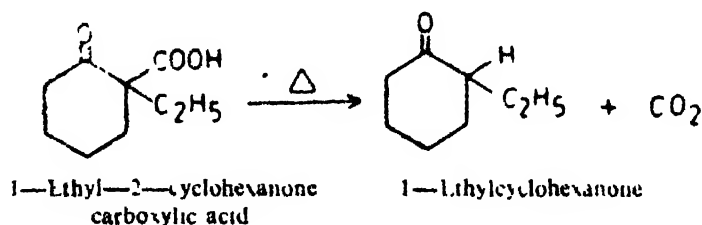


c. Reactions Involving the Carboxyl Group

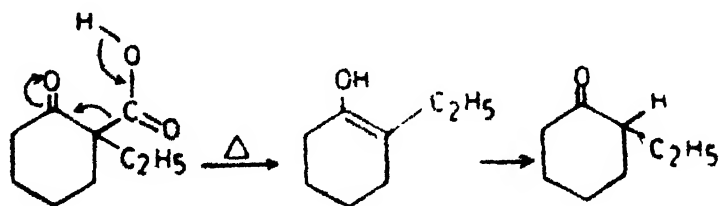
1. **Decarboxylation:** Sodium salts of the acid, on fusion with soda lime ($\text{NaOH} + \text{CaO}$), suffer loss of carbon dioxide and the corresponding hydrocarbon is obtained



A carboxylic acid can be decarboxylated without soda lime if it contains a β -carbonyl group or a β, γ - $\text{C}=\text{C}$ bond as shown below:

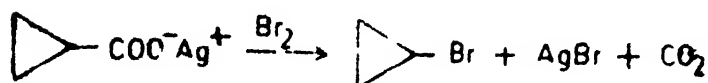
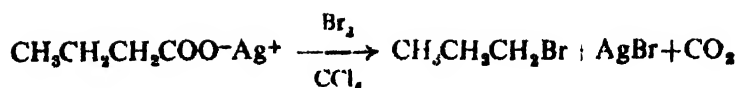


Mechanism



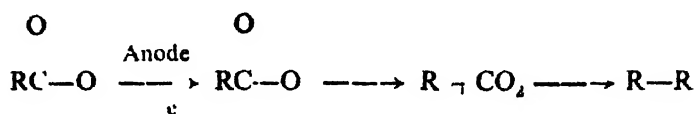
2. **Hunsdiecker Reaction:** Carboxylic acids form silver salts by treating its ammoniacal solution with silver nitrate. The salt, on refluxing with bromine, forms an alkyl bromide. This is known as the *Hunsdiecker reaction*.





The reaction is believed to proceed *via* a free radical chain mechanism

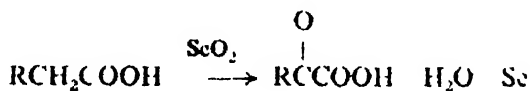
3. *Kolbe's Electrolysis*: In this reaction an aqueous solution of sodium or potassium salt of the acid is subjected to electrolysis.



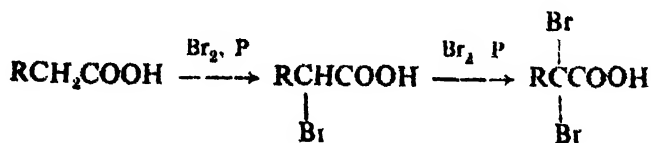
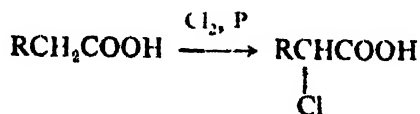
At the anode the carboxylate ion loses an electron to become a radical, which on decarboxylation and coupling forms an alkane.

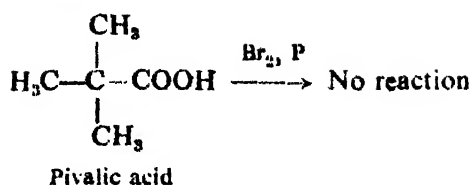
d. *Reactions Involving the Aliphatic Moiety*

1 Carboxylic acid can be oxidized by selenium dioxide, SeO_2 , at the α -methylene group to yield a keto acid.



2. *Hell-Volhard Zelinsky Reaction* Hydrogen atoms on an α -carbon atom can, in an aliphatic acid, readily be replaced with chlorine or bromine in the presence of a catalytic quantity of red phosphorus and the respective halogen (Br_2 or Cl_2). The reaction is facilitated by using phosphorus tribromide. The second hydrogen may be replaced by using excess of the halogen. If there are no such hydrogens available, the reaction does not proceed. For instance, pivalic acid does not react under these conditions.

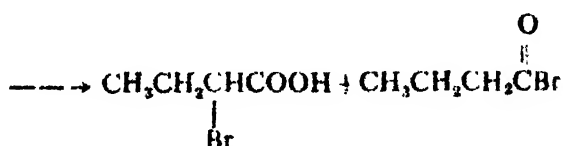
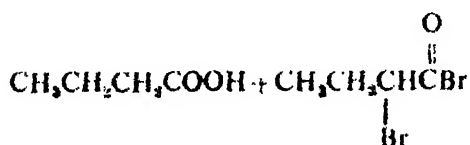
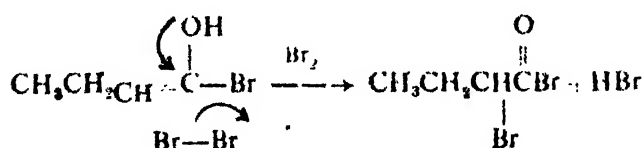
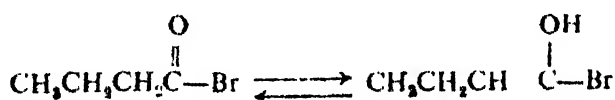
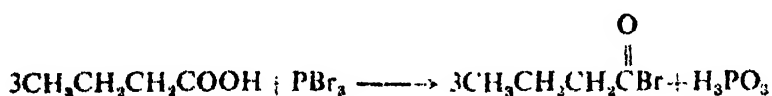




The reaction can be employed for structure determination and in the synthesis of α -amino acids.

Mechanism

The reaction is not a free radical chain process. Phosphorus tribromide or trichloride helps to convert the acid into an acyl halide. The important step is the reaction of bromine with the enol form of the acyl bromide. The acyl bromide undergoes enolization much more readily than the acid itself:



Section B: UNSATURATED CARBOXYLIC ACIDS

Carboxylic acids and their derivatives containing a $\text{C}=\text{C}$ bond are well-known natural compounds, oleic acid $[\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}]$

is present in olive oil. Many of them are known by their common names, however, IUPAC names may also be given to the complicated members. Physical constants of some acids are given in Table 18.2

Table 18.2 Physical Constants of Unsaturated Acids

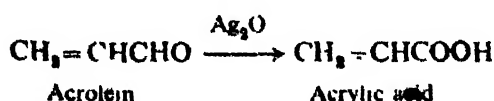
Acids	Common Name	IUPAC Name	m.p. (°C)	b.p. (°C)
$\text{H}_2\text{C}=\text{CHCOOH}$	Acrylic acid	2—Propenoic acid	12	142
$\text{CH}_3\text{CH}=\text{CHCOOH}$	<i>trans</i> —Crotonic acid	<i>trans</i> —But—2—enoic acid	72	189
$\text{C}_6\text{H}_5\text{CH}=\text{CHCOOH}$	<i>trans</i> —Cinnamic acid	<i>trans</i> —3—Phenyl—propenoic acid	137	300
$\begin{array}{c} \text{H} \quad \text{COOH} \\ \diagdown \quad \diagup \\ \text{C} \end{array}$	Maleic acid	<i>cis</i> —Butenedioic acid	130.5	—
$\begin{array}{c} \text{C} \\ \diagup \quad \diagdown \\ \text{H} \quad \text{COOH} \end{array}$				
$\begin{array}{c} \text{H} \quad \text{COOH} \\ \diagdown \quad \diagup \\ \text{C} \\ \\ \text{C} \\ \diagup \quad \diagdown \\ \text{HOOC} \quad \text{H} \end{array}$	Fumaric acid	<i>trans</i> —Butenedioic acid	32	—

18.6 PREPARATION OF UNSATURATED ACIDS

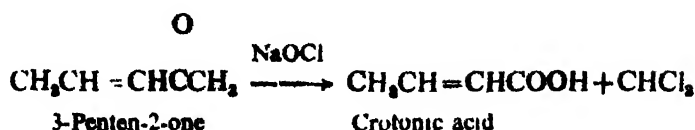
Unsaturated carboxylic acids are prepared by the following general methods.

1. *Oxidation of Acrolein*: Oxidation of acrolein by silver oxide leads to acrylic acid. Silver oxide is a mild and selective oxidizing agent as it does

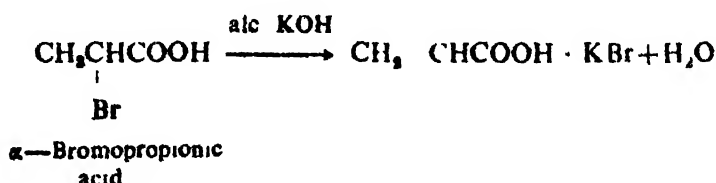
not touch the $\begin{array}{c} \diagup \quad \diagdown \\ \text{C}=\text{C} \\ \diagdown \quad \diagup \end{array}$ double bond.



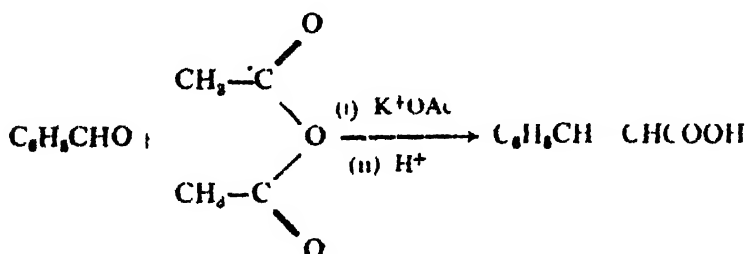
Unsaturated methyl ketones are oxidized by hypohalite, i.e. the haloform reaction, to carboxylic acids.



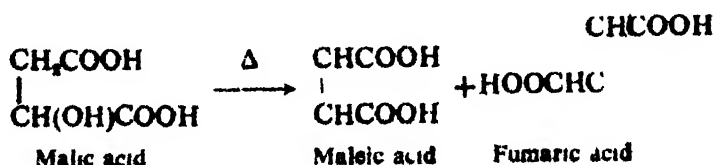
2. *Dehydrohalogenation of α -Halo Acids:* Unsaturated acids can be obtained by elimination of a molecule of HX in the presence of alc. KOH from an α -halo acid. The α -halo acid can be prepared by the Hell-Volhard Zelinsky reaction,

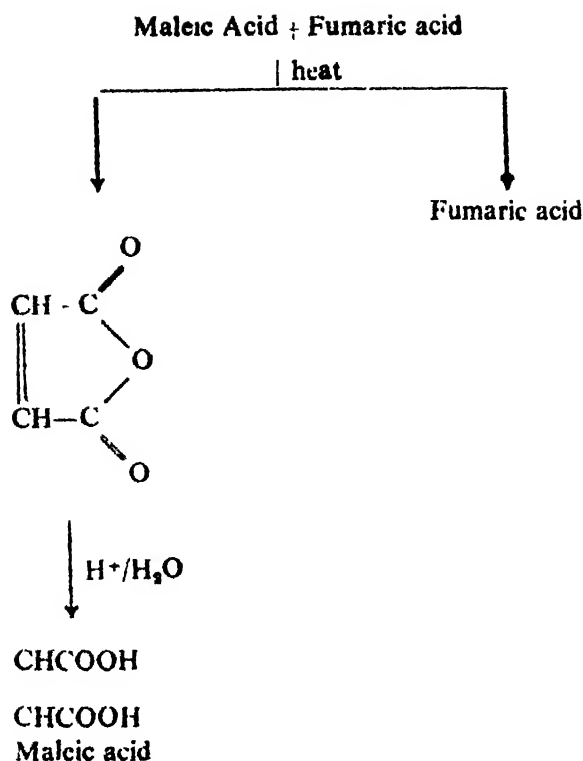


3. *Perkin Reaction:* This is the most commonly used laboratory method for the preparation of cinnamic acid and its derivatives

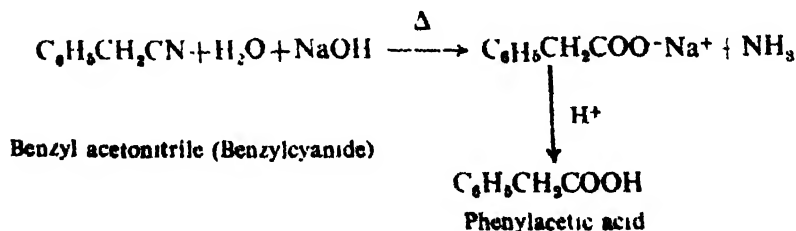
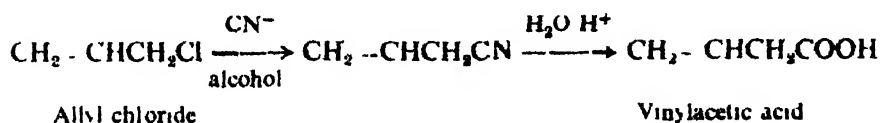


4 Both maleic and fumaric acids may be prepared from malic acid on heating. In the mixture, maleic acid being *cis* forms an anhydride and thus can be separated from fumaric acid.





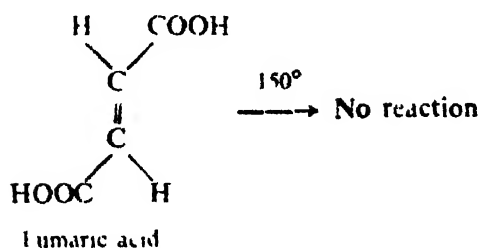
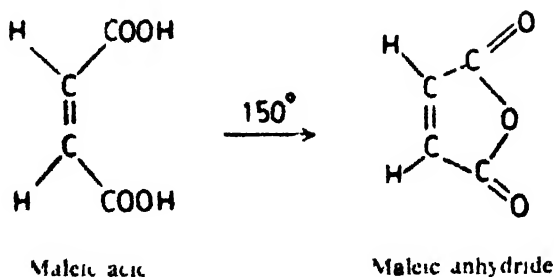
5. *Hydrolysis of Unsaturated Nitriles* Nitriles which may be obtained by the S_N2 displacement of a halogen by a cyanide ion which on hydrolysis yield carboxylic acids.



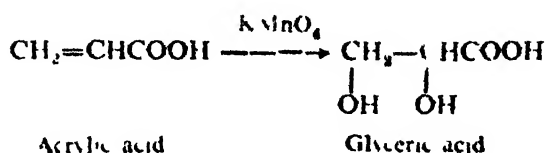
18.7 REACTIONS OF UNSATURATED ACIDS

1. *Addition to $\text{C}=\text{C}$ Bond*: Various reagents adds to the $\text{C}=\text{C}$ bond of unsaturated acids to form useful derivatives.

3. *Dehydration*: Maleic acid loses a molecule of water on heating at 150° but the isomeric is recovered unchanged.



4. *Oxidation*: With dil KMnO_4 , acrylic acid is oxidized to glyceric acid



Section C : HYDROXY CARBOXYLIC ACIDS

Hydroxy carboxylic acids contain at least one $-\text{OH}$ group attached to the hydrocarbon chain. Many of them occur naturally, for instance, tartaric acid (in grapes) citric acid (in citrus fruits), glycolic acid (a constituent of cane sugar) and maleic acid (occurs in fruit juice). Hydroxy acids are often given the trivial names (Table 18.3). The hydroxy group may be present either of the α , β or γ position.

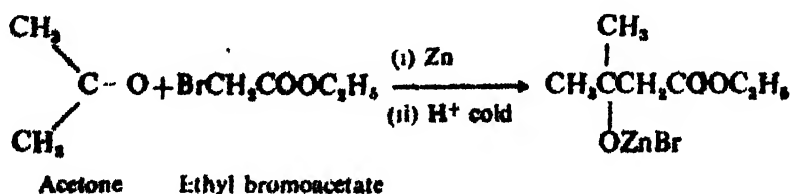
Table 18.3 Physical Constants of Hydroxy Acids

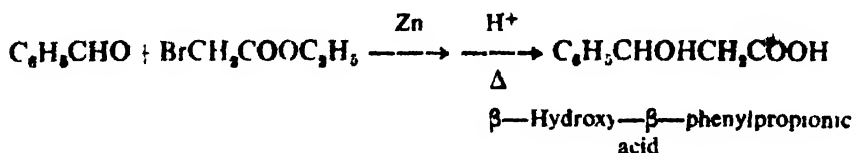
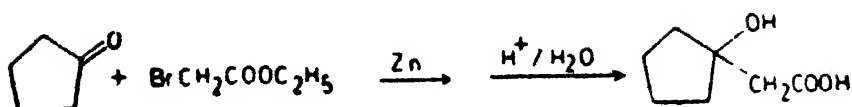
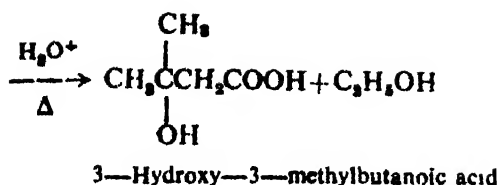
Acid	Name	m p ($^{\circ}\text{C}$)
HOCH_2COOH	Glycolic acid	80
$\begin{array}{c} \text{CH}_3\text{CHCOOH} \\ \\ \text{OH} \end{array}$	Lactic acid	52
$\begin{array}{c} \text{C}_6\text{H}_5\text{CHCOOH} \\ \\ \text{OH} \end{array}$	Mandelic acid	120
$\begin{array}{c} \text{CH}_2-\text{CHCOOH} \\ \quad \\ \text{OH} \quad \text{OH} \end{array}$	Glyceric acid	—
$\begin{array}{c} \text{CH}(\text{OH})\text{COOH} \\ \\ \text{CH}_2\text{COOH} \end{array}$	(—) Maleic acid	101
$\begin{array}{c} \text{CH}(\text{OH})\text{COOH} \\ \\ \text{CH}(\text{OH})\text{COOH} \end{array}$	Tartaric acid	170
$\begin{array}{c} \text{CH}_2\text{COOH} \\ \\ \text{C} \begin{array}{l} \nearrow \text{OH} \\ \searrow \text{COOH} \end{array} \\ \\ \text{CH}_2\text{COOH} \end{array}$	Citric acid	135

18.3 PREPARATION OF HYDROXY CARBOXYLIC ACIDS

Hydroxy acids may be prepared by the following general methods.

1. *Reformatsky Reaction*: An aldehyde or ketone reacts with an α -bromo ester and metallic zinc to yield a β -hydroxy acid. This is called the *Reformatsky reaction*.

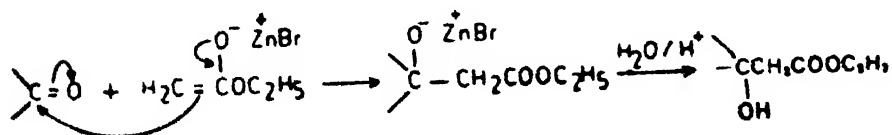
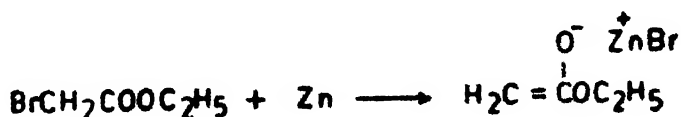




Zinc is preferred to Mg because the Grignard reagent will react with ester ($\text{BrCH}_2\text{COOC}_2\text{H}_5$).

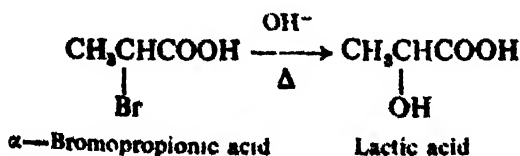
Mechanism

The mechanism of the reaction begins with the formation of an organozinc reagent and may be considered as the anion of the ester. This carbanion makes a nucleophilic attack on the carbonyl group of an aldehyde or ketone

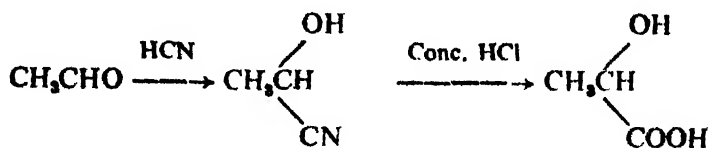


This on hydrolysis on heating yields the acid.

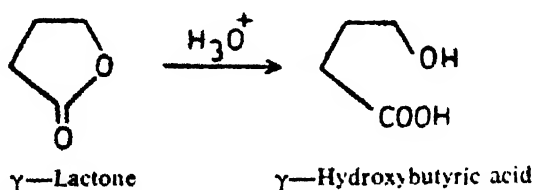
2. *Hydrolysis of α-Halocarboxylic acids:* A α-halocarboxylic acid prepared by the Hell-Volhard-Zelinsky procedure on hydrolysis forms an hydroxy acid.



3. *Hydrolysis of Cyanohydrins*: This is the most general method for the preparation of hydroxy acids. Both the —OH and —COOH groups are introduced according to the following sequence of reactions.



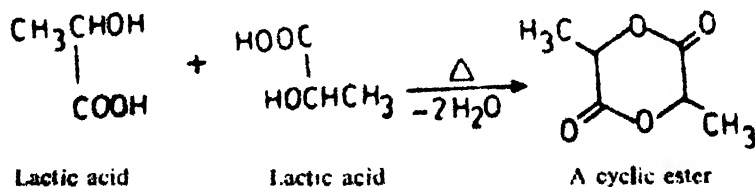
4. *Hydrolysis of Lactones*: Hydrolysis of lactones is another method for obtaining hydroxy acids. A γ -lactone, on hydrolysis, for instance, results in γ -hydroxy butyric acid.



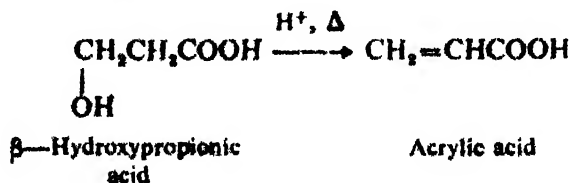
18.9 REACTIONS OF HYDROXY ACIDS

1. *Dehydration*: This is the most important reaction of hydroxy acids. They undergo dehydration in the presence of an acid or on heating. Three types of acids (α , β or γ hydroxy) lead to different products and this can thus serve as a test to distinguish them.

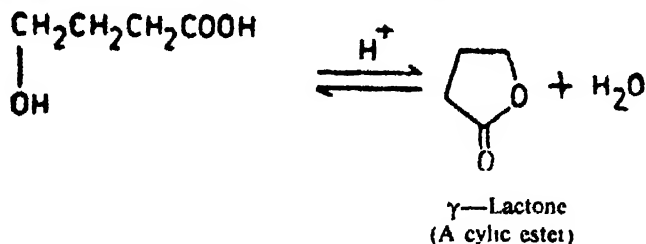
a. *α -Hydroxy Acids*: α -Hydroxy acids are not capable of forming a stable lactone but undergo intermolecular self-esterification. The final cyclic product containing two carbonyl groups is called a *lactide*.



b. *β -Hydroxy Acids*: A β -hydroxy acid loses a molecule of water to yield an unsaturated carboxylic acid. The dehydration can be brought about by heating with an acid.

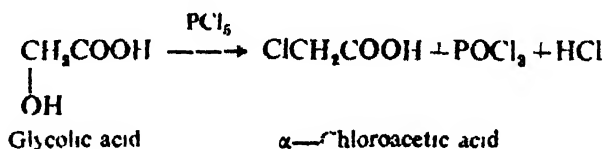


c. *γ -Hydroxy Acids*: A lactone, i.e. a cyclic ester is obtained in this case. Lactonization occurs rapidly to yield an equilibrium mixture.



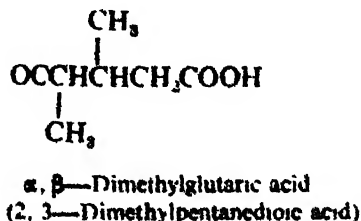
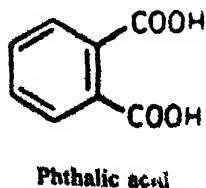
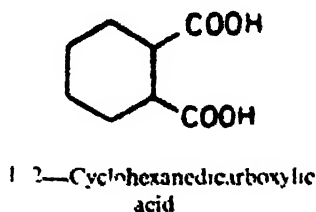
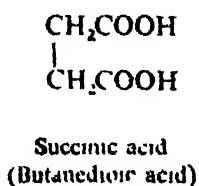
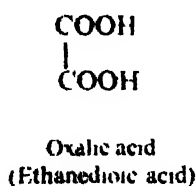
It is a reversible process as the hydrolysis of lactones affords hydroxy acids. However, if the lactone formed is stable, i.e., five or six membered ring lactones, then a substantial amount of the lactone is formed. Larger ring lactones are difficult to prepare because of the less probability of ring closure.

2. *Reaction with PCl_5* : The —OH group can be replaced by Cl in the presence of phosphorus pentachloride.



Section D: DICARBOXYLIC ACIDS

A dicarboxylic acid contains two carboxyl functions attached to the same or different carbon atoms. All dicarboxylic acids are solids and the lower members are soluble in water. Aliphatic dicarboxylic acids are named as alkanedioic acids in the IUPAC system. They are also given common names.





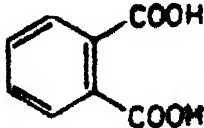
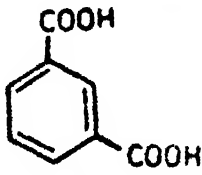
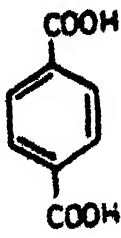
Butanedioic acid



3-(Carboxymethyl) hexanoic acid

Physical constants of the acids are listed in Table 18.4.

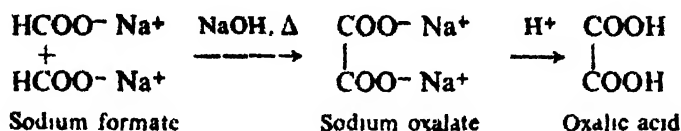
Table 18.4 Physical Constants of Dicarboxylic acids

Formula	Name	$K_1 \times 10^5$	$K_2 \times 10^5$	m.p. ($^{\circ}\text{C}$)
Oxalic acid	$\text{HOOC}-\text{COOH}$	3500	5.3	189
Malonic acid	$\text{HOOCCH}_2\text{COOH}$	171	.22	136
Succinic acid	$\text{HOOC}(\text{CH}_2)_2\text{COOH}$	676	0.75	185
Glutaric acid	$\text{HOOC}(\text{CH}_2)_3\text{COOH}$	4.7	0.29	98
Adipic acid	$\text{HOOC}(\text{CH}_2)_4\text{COOH}$	3.7	0.24	151
Pimelic acid	$\text{HOOC}(\text{CH}_2)_5\text{COOH}$			105
Suberic acid	$\text{HOOC}(\text{CH}_2)_6\text{COOH}$			144
Azelic acid	$\text{HOOC}(\text{CH}_2)_7\text{COOH}$			106
Sebacic acid	$\text{HOOC}(\text{CH}_2)_8\text{COOH}$			174
Phthalic acid		130	39	231
iso-Phthalic acid		29	2.5	348.5
Terephthalic acid		11	1.5	300 (sub)

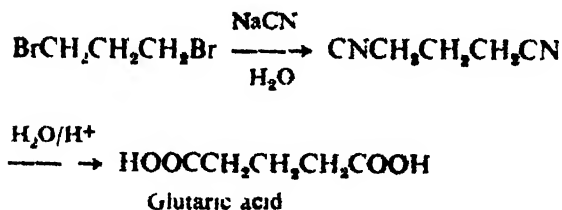
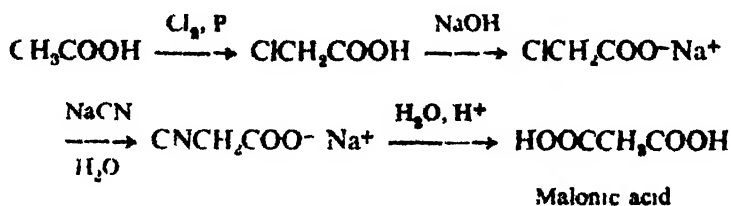
The inductive effect of one carboxyl group is expected to enhance the acidity of the other -COOH group. The acid dissociation constant K_1 is higher than K_2 .

18.10 PREPARATION OF DICARBOXYLIC ACIDS

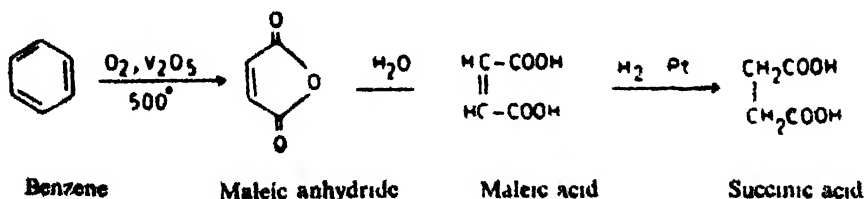
1. The first member of the series, i.e., oxalic acid is prepared by heating sodium formate in the presence of an alkali. Oxalic acid crystallizes out from water as a dihydrate.



2. Several of the dicarboxylic acids are obtained by the hydrolysis of the corresponding cyanides.

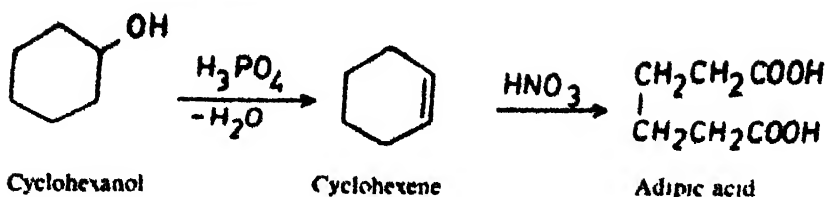


3. Succinic acid is prepared from maleic anhydride which in turn is obtained from benzene by its drastic oxidation.

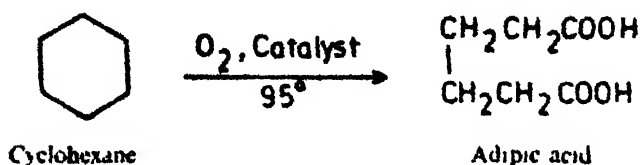


4. Adipic acid is obtained commercially by a number of methods.

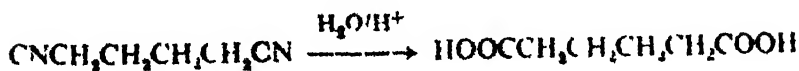
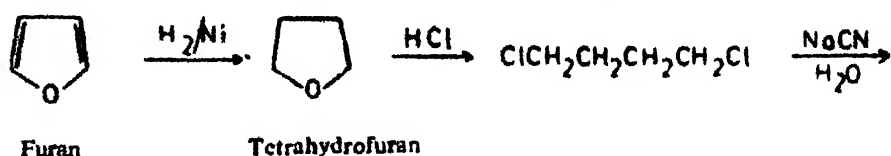
a. Oxidation of cyclohexene:



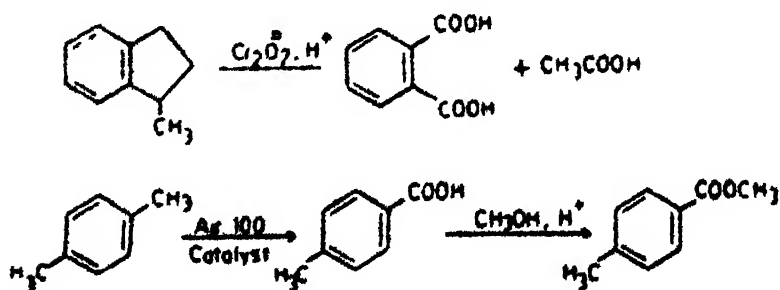
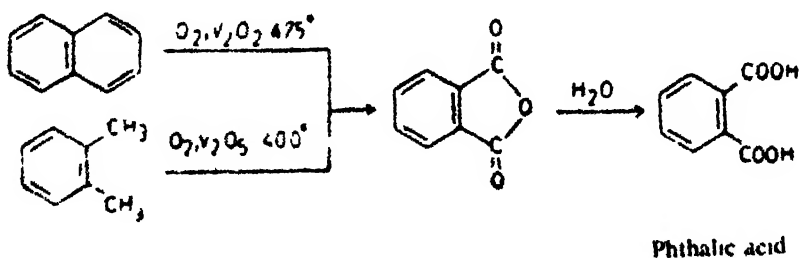
b. Oxidation of cyclohexane:

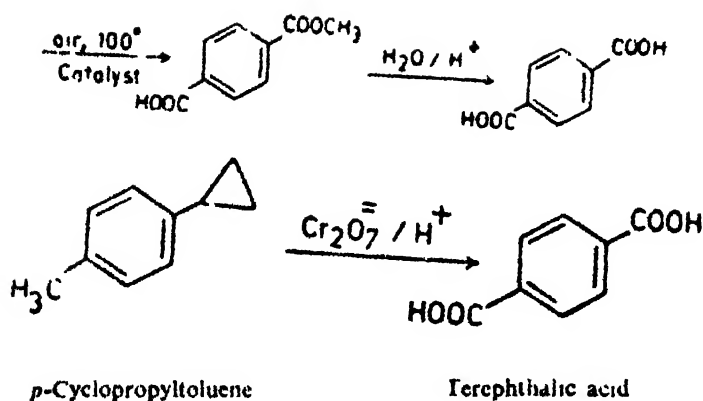


c. From tetrahydrofuran (THF) by the following sequence of reactions



5. Aromatic dicarboxylic acids are obtained by the direct oxidation of hydrocarbons:





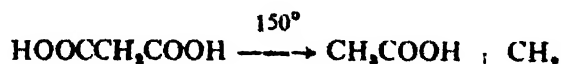
18.11 REACTIONS OF DICARBOXYLIC ACIDS

Dicarboxylic acids, in general display the same chemical behavior as mono-carboxylic acids. For instance, they can be converted into sodium

salts $\left(\begin{array}{c} \text{COO}^-\text{Na}^+ \\ | \\ \text{COO}^-\text{Na}^+ \end{array} \right)$, acid chlorides $\left(\begin{array}{c} \text{COCl} \\ | \\ \text{COCl} \end{array} \right)$, amides $\left(\begin{array}{c} \text{CONH}_2 \\ | \\ \text{CONH}_2 \end{array} \right)$,

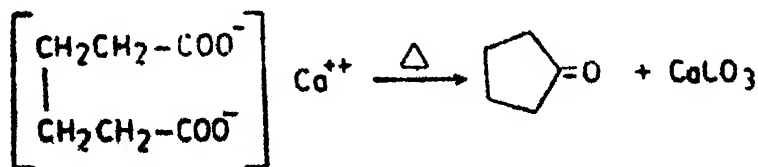
esters $\left(\begin{array}{c} \text{COOCH}_3 \\ | \\ \text{COOCH}_3 \end{array} \right)$ and anhydrides $\left(\begin{array}{c} \text{O} \\ // \quad \backslash \\ \text{C} \quad \text{C} \\ | \quad | \\ \text{O} \quad \text{O} \end{array} \right)$

1. *Action of Heat:* Malonic acid suffers decarboxylation on heating to yield acetic acid.



Succinic, glutaric and phthalic acids lose water to form anhydrides.

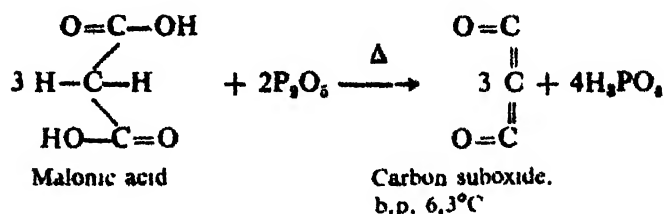
2. *Action of Heat on Calcium Salt:* Calcium salts of higher dicarboxylic acids, form cyclic ketones, on heating strongly.



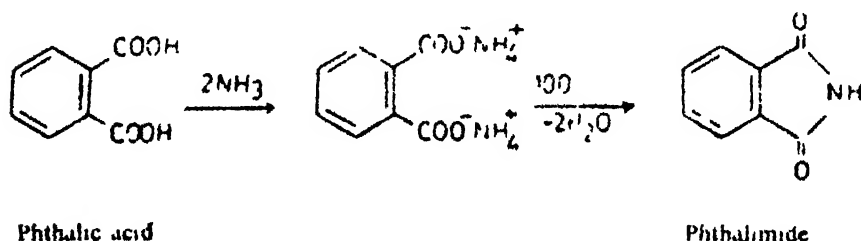
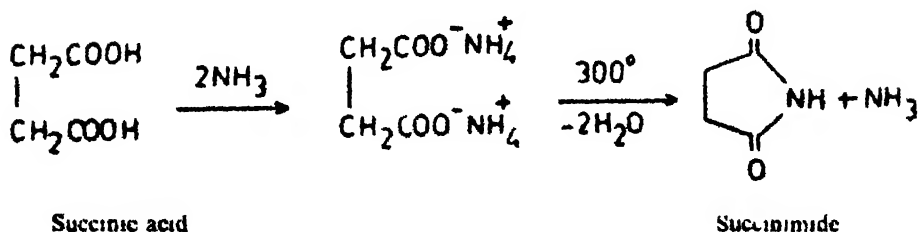
Calcium adipate

Cyclopentanone

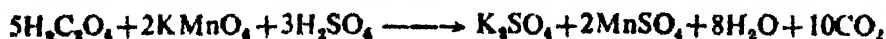
4. Malonic acid, on heating with P_2O_5 , forms carbon suboxide.



5. Succinic, glutaric and phthalic acids form imides with ammonia.

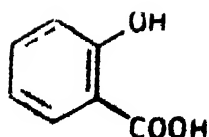
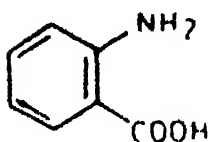
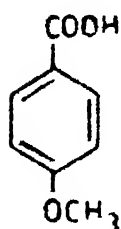
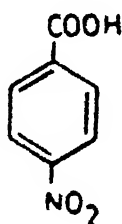
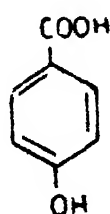


6. A hot solution of pot. permanganate quantitatively oxidizes oxalic acid according to the following equation.

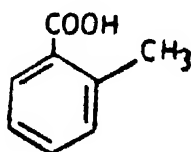
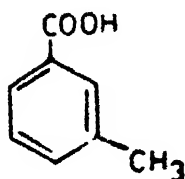
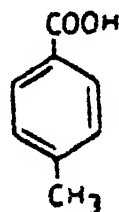


Section E: AROMATIC CARBOXYLIC ACIDS

A carboxylic function ($-\text{COOH}$) is linked to an aromatic residue in an aromatic carboxylic acid. The common names of several aromatic carboxylic acids resemble the names of the parent aromatic hydrocarbons, for instance, benzene and benzoic acid, naphthalene and naphthoic acid, etc. Substituted benzoic acids are either named with the prefixes *ortho*, *meta* or *para* or using a numeral, in which case the carbon atom carrying the carboxyl group is numbered as 1. Several of these acids also have common names.

*o*-Hydroxybenzoic acid (Salicylic acid)*o*-Aminobenzoic acid (Anthranilic acid)*p*-Methoxybenzoic acid
(Anisic acid)*p*-Nitrobenzoic acid*p*-Hydroxybenzoic acid

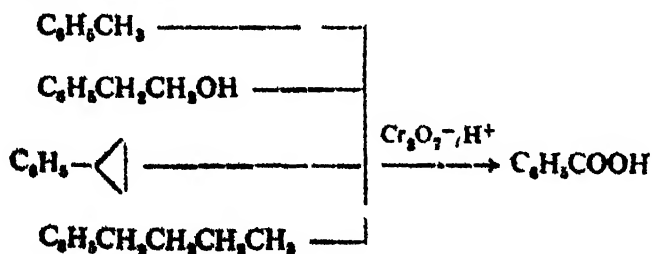
The methyl benzoic acids are given the special names of toluic acids.

*o*-Toluic acid*m*-Toluic acid*p*-Toluic acid

Aromatic carboxylic acids are crystalline solids. Several of them are miscible with water but are readily soluble in most organic solvents.

18.12 PREPARATION OF AROMATIC CARBOXYLIC ACIDS

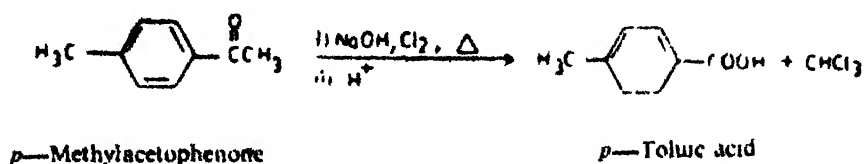
1. *Oxidation*: The aromatic carboxylic acids are obtained by oxidation of the side chain of the benzene ring since the latter is sufficiently stable toward oxidising agents.



Alkaline pot. permanganate may also be employed as an oxidizing agent.

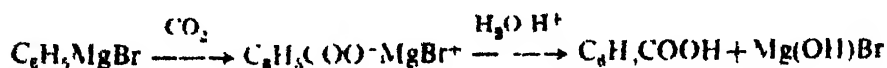
It may be noticed that in the oxidation of the side chain, it is oxidized all the way back to the carbon atom linked to the aromatic ring.

2. *The Haloform Reaction:* This is an important procedure for the preparation of carboxylic acids from methyl ketones.

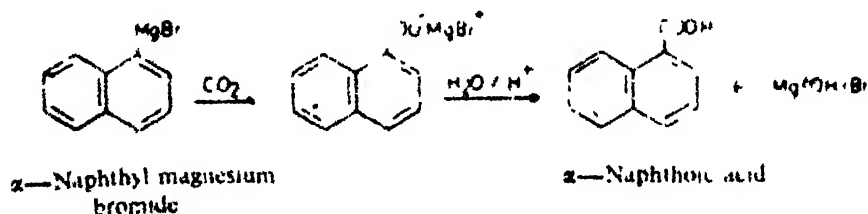


In contrast to the preceding method only one carbon atom is oxidised in the reaction.

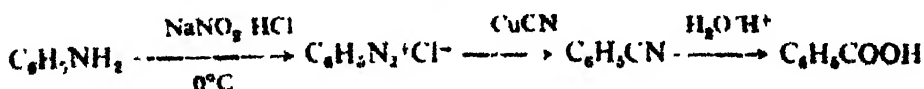
3. *Grignard Reagents:* The carbonation of Grignard reagents is a useful method for preparing carboxylic acids. Benzoic acid may be obtained from phenyl magnesium bromide.



α -Naphthoic acid is obtained in a similar manner



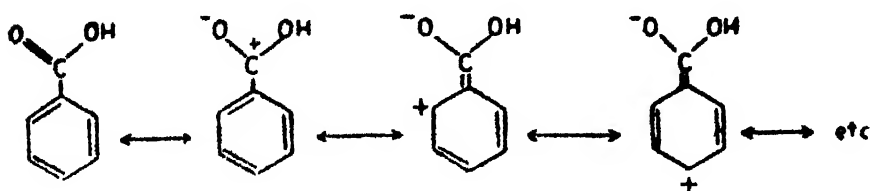
4. *Hydrolysis of Nitriles.* This is highly useful method for the preparation of carboxylic acids and employs nitriles as intermediates.



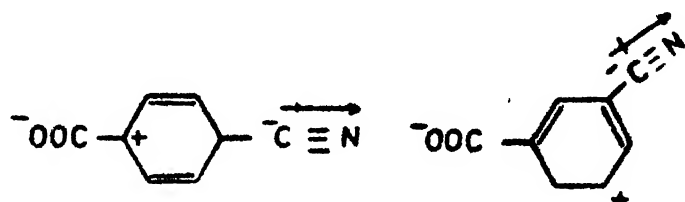
18.13 ACIDITY OF BENZOIC ACIDS

Aromatic carboxylic acids are slightly more acidic than the aliphatic acids. This is attributed to the fact that the sp^2 hybridized carbon atom of the benzene ring is more electronegative than the sp^3 hybridized carbon atom in an aliphatic chain. The phenyl group thus functions as an electron-withdrawing group. In the phenoxide ion, the charge resides partly on the benzene ring due to resonance and as a result, phenol is more acidic than ethanol. In the same manner one would expect that linking the $-\text{COOH}$ group directly to the benzene ring would augment the acidity of benzoic acid and make it

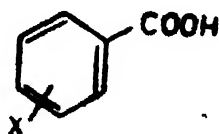
stronger than acetic acid. However, the difference is much less; for benzoic acid, $K_a = 6.5 \times 10^{-5}$ and for acetic acid, $K_a = 1.8 \times 10^{-5}$ because the acid itself is stabilized by resonance.



This type of conjugation is less effective in the case of the benzoate ion than the phenoxide ion so the contribution of the aromatic ring to increase the acidity is less than in the case of phenol. The presence of electron-withdrawing groups in benzoic acid stabilizes the anion and thus increase the value of the ionization constant. This is due to the polarization of the following type.



The electron-donating groups have the opposite effect, because they tend to destabilize the anion and thus localize the negative charge on the carboxylate anion. This increases the tendency of the ion to regain the proton. The PK_a values of some substituted benzoic acids are given below:



Substituent	ortho	meta	para
NO_2	2.21	3.49	3.42
OCH_3	4.09	4.09	4.47
OH	2.98	4.08	4.57
CN	3.14	3.64	3.55
Br	2.85	3.81	3.97
Cl	2.92	3.83	3.97
CH_3	3.91	4.27	4.38
H	4.20	4.20	4.20

As is evident from the above values, the introduction of an alkyl group has very little effect on the strength of benzoic acid. Electron-withdrawing groups, however, enhance the acidity. This effect is more pronounced when such groups are present in the *ortho* and *para* positions. The electron withdrawing effect of *o*-NO₂ group is particularly quite considerable which may be due to the short distance over which the powerful inductive effect of this group is operating.

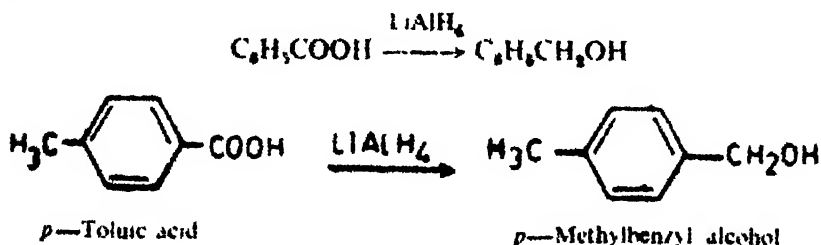
The presence of groups such as —OCH₃, —OH or halogens which are electron-withdrawing inductively but electron-donating mesomerically when present in *o*— and *p*—positions may even cause the *p*—substituted acids to be weaker than the *m*—substituted acids.

It may also be noticed that the behavior of some *o*—substituted benzoic acids is anomalous and the acid strength is considerably higher than expected. This is due to the interaction of the group with the adjacent carboxyl group, i.e. intramolecular hydrogen-bond formation.

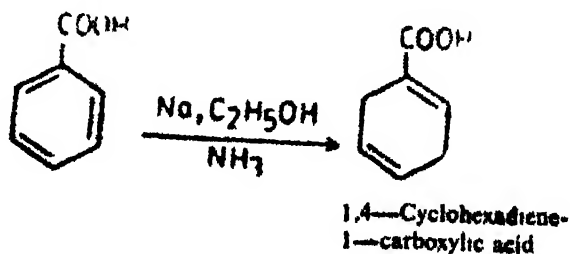
18.14 REACTIONS OF AROMATIC CARBOXYLIC ACIDS

1. Aromatic carboxylic acids, in a manner similar to aliphatic acids form salts with NaHCO₃ and NaOH, acid chlorides with PCl₅ or SOCl₂, esters with alcohols, amides with ammonia and anhydrides on heating.

2. *Reduction*: The carboxyl group, analogous to the ester function is also reduced to a primary alcohol with LiAlH₄.

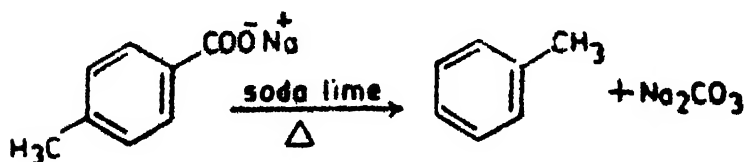
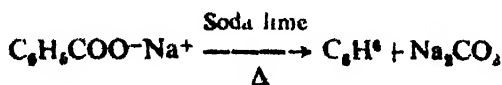


The aromatic ring can be reduced under the Birth conditions, i.e., by alkali metals in a mixture of liquid ammonia and alcohol. The reduced product is an unconjugated cyclohexadiene. No further reduction takes place and the product is isolated in good yields.

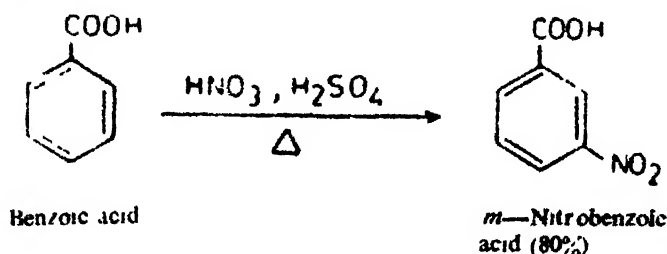


3. *Decarboxylation*: Carboxylic acids evolve carbon dioxide on treat-

ment with sodium bicarbonate. The sodium salt of the acid on heating with soda lime undergoes the loss of carbon dioxide to yield a hydrocarbon.



4. *Ring Substitution*: The carboxyl group is electron-withdrawing and is thus *meta* directing.



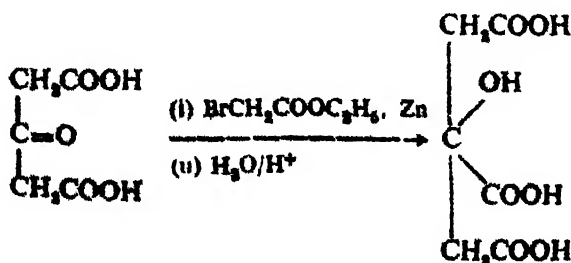
18.15 INDIVIDUAL ACIDS

18.15.1 Citric Acid

Citric acid is a hydroxy tricarboxylic acid and occurs widely in lemon, lime and other citrus fruits. It is an important intermediate in carbohydrate metabolism.

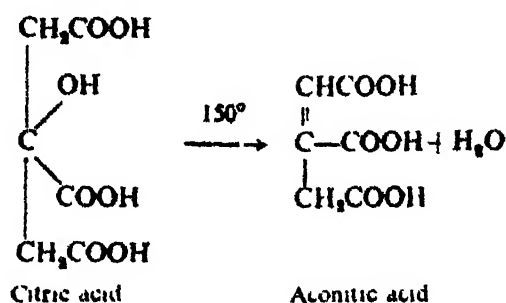
Preparation

1. The acid is obtained by boiling the fruit juices and then neutralizing it with calcium carbonate. Calcium citrate so obtained is decomposed by sulfuric acid to obtain citric acid.
2. It may be obtained from acetonedicarboxylic acid and ethyl bromoacetate ($\text{BrCH}_2\text{COOC}_2\text{H}_5$) by the Reformatsky reaction.



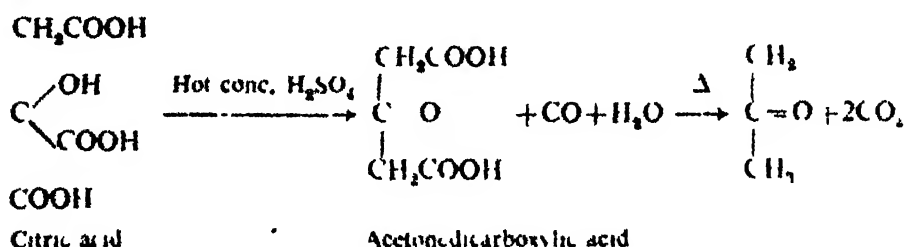
Reactions:

1. On heating, to 150° , citric acid forms aconitic acid by splitting a molecule of water intramolecularly.



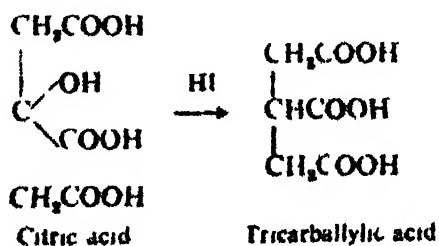
2. It forms salts with alkalis, esters with alcohols, chlorides with PCl_5 or SOCl_2 , and amides, with ammonia.

3. With hot conc. sulfuric acid, citric acid loses carbon monoxide and water and forms acetonedicarboxylic acid



which on further heating forms acetone and carbon dioxide

4. Treatment of citric acid with hydroiodic acid yields tricarballic acid,



Citric acid and tartaric acid differ in their following properties.

- Citric acid is optically inactive while tartaric acid shows optical activity
- Citric acid, on heating at 150° , forms aconitic acid while tartaric acid yields tartaric anhydride.
- With HI , citric acid yields tricarballic acid while tartaric acid forms succinic acid.

USES

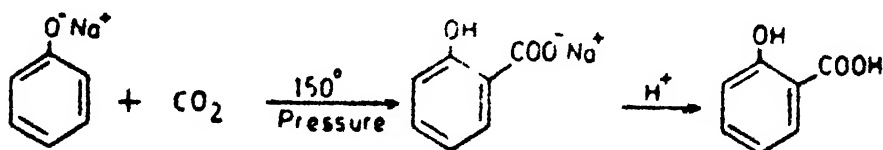
Citric acid esters find use as plasticizers. The acid itself is added to soft drinks and candies. It is also employed in the dye industry.

18.152 Salicylic Acid

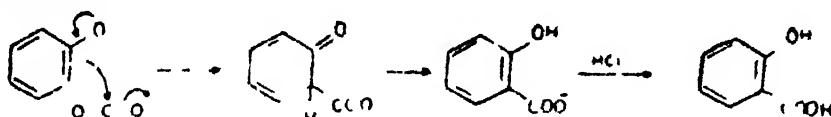
The most important of the phenolic acids is the salicylic acid (*o*-hydroxybenzoic acid).

Preparation

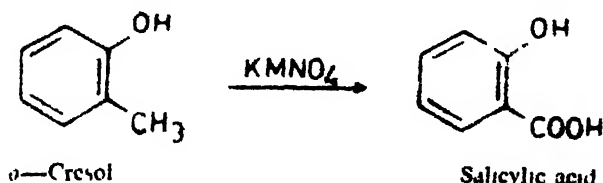
1. Salicylic acid is prepared by the Kolbe's reaction which involves the reaction of phenoxide ion with carbon dioxide to yield sodium salicylate



The acid is regenerated by treatment with HCl

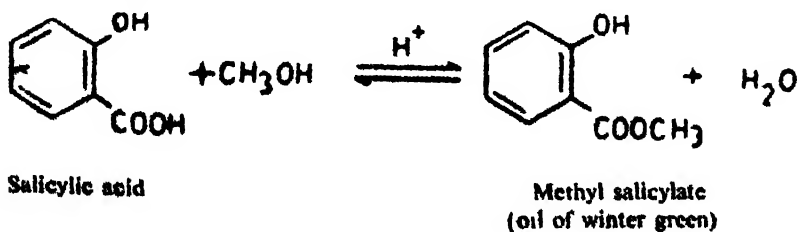
Mechanism

2. It may also be obtained by the oxidation of *o*-cresol

**Reactions**

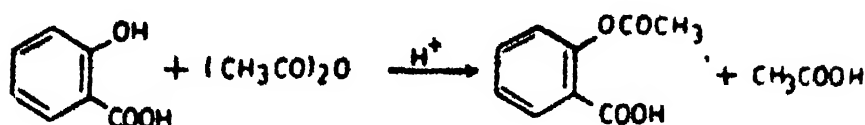
Salicylic acid behaves chemically similar to aromatic carboxylic acids and gives reactions of both phenol as well as the carboxyl group.

1. Salicylic acid forms sodium salt alkalis. With methanol it is esterified to give methyl salicylate. It is a pleasant smelling oil and is used in making ointments such as *iodex*.



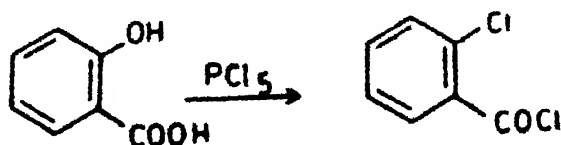
The phenyl ester of salicylic acid is known as *salol*.

2. The phenolic group is acetylated with acetic anhydride to form acetyl salicylate.

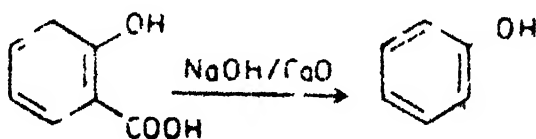


The sodium salt of acetyl salicylate is known as *aspirin*.

3. With phosphorus pentachloride, salicylic acid forms *o*-chlorobenzoyl chloride.



4. On heating with soda-lime the acid yields phenol.



USES

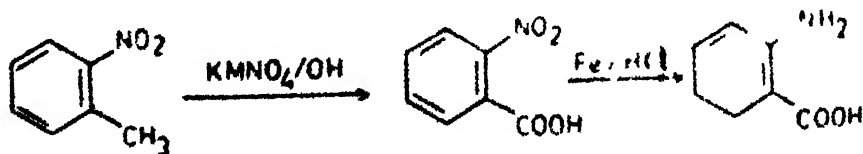
Salicylic acid derivatives are used in medicines. Salol is used in coating pills in order to permit their contents to pass into the intestines. Aspirin is used widely because of its analgesic (pain killing) properties.

18.15.3 Anthranilic Acid

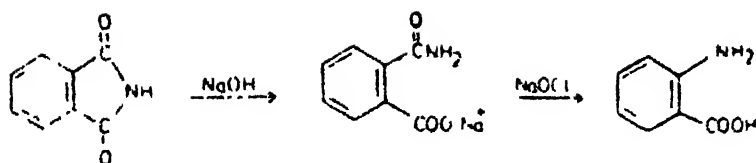
It is an *o*-amino derivative of benzoic acid.

Preparation

1. Anthranilic acid may be prepared from *o*-nitrotoluene by the following sequence :



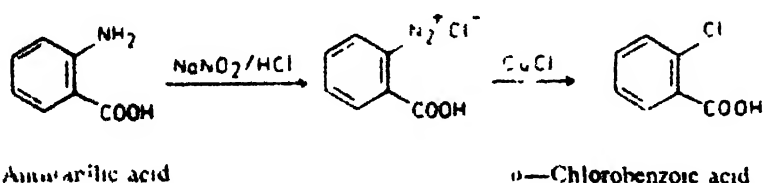
2. Commercially, it is obtained by reacting phthalimide with alkaline sod. hypochlorite,



Anthranilic acid is a colorless crystalline substance, m.p. 145° and is soluble in water, alcohol or ether

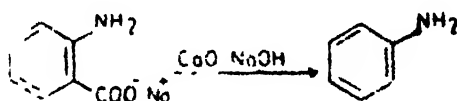
Reactions

1. The amino group of anthranilic acid undergoes the Sandmeyer reaction.

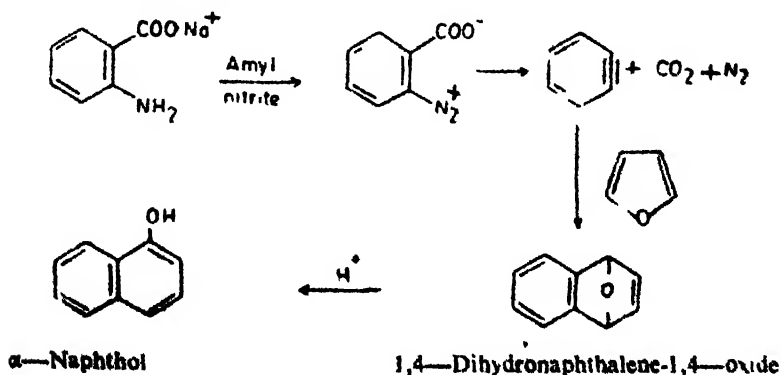


2. Like other carboxylic acids, the carboxyl group of the acid forms esters with alcohols, salts with sodium hydroxide and amides with ammonia.

3. The sodium salt, of anthranilic acid, on fusion with soda lime, yields aniline



4. The diazonium benzoate, obtained from anthranilic acid is of particular interest because it readily decomposes to benzyne on warming. This undergoes the Diels-Alder reaction with furan.



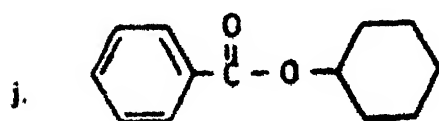
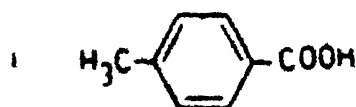
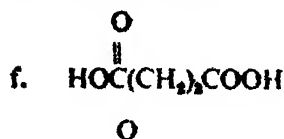
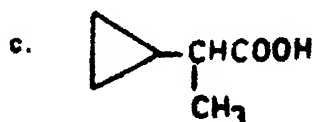
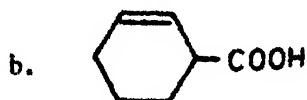
USES

Mefenamic acid, a derivative of anthranilic acid is used as an antiinflam-

matory agent. Anthranilic acid is used in the preparation of indigo and in perfumery.

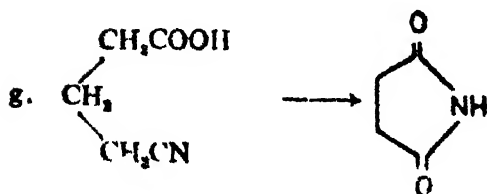
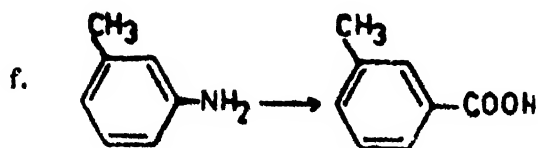
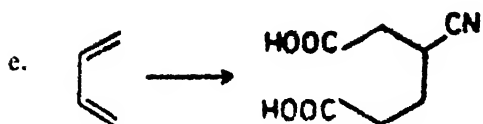
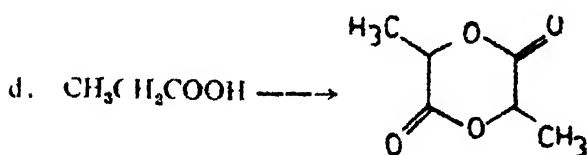
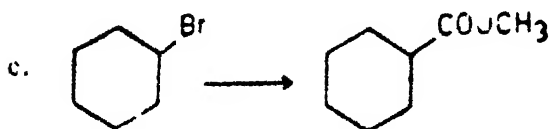
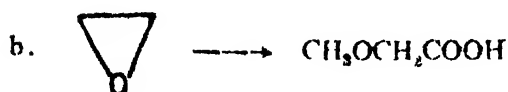
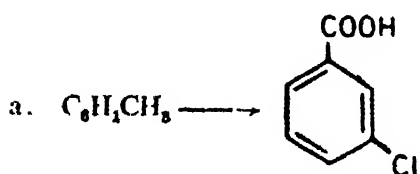
QUESTIONS

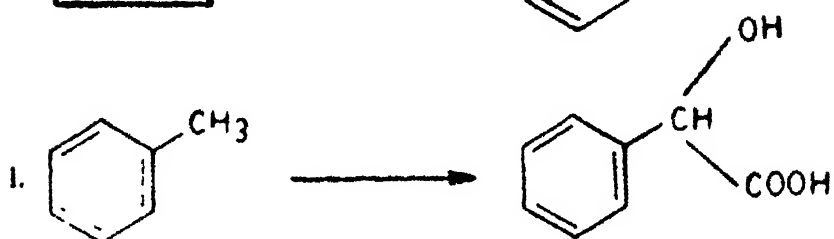
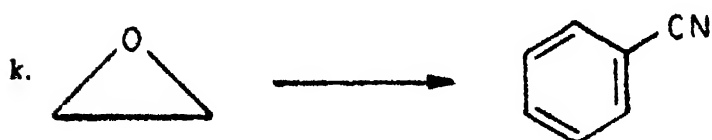
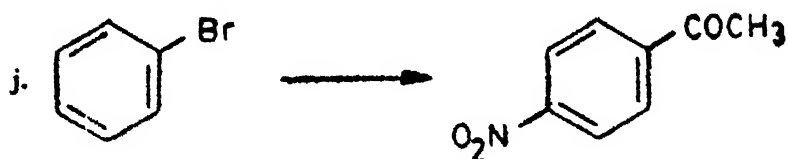
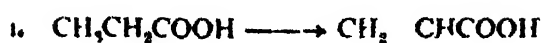
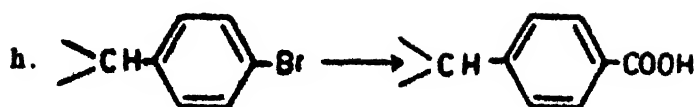
18.1 Give IUPAC name for each of the following compounds:



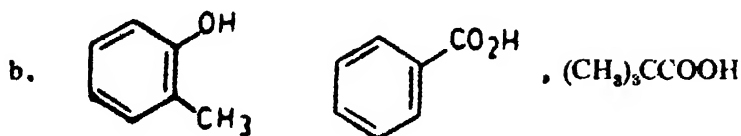
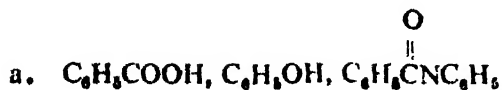
18.2 Discuss the action of heat on hydroxy carboxylic acids.

18.3 How will you effect the following conversions?

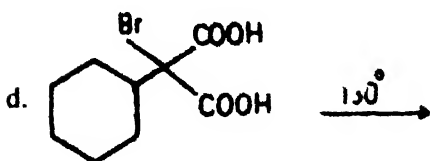
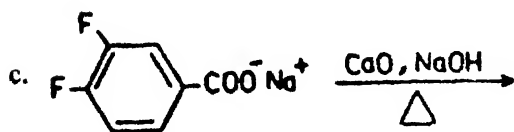
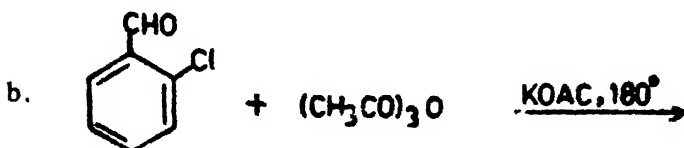
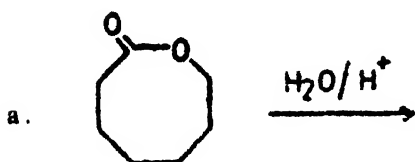


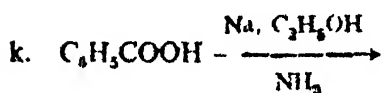
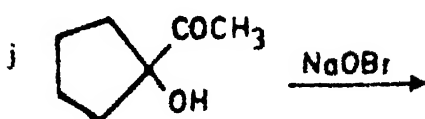
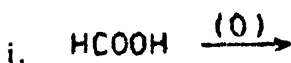
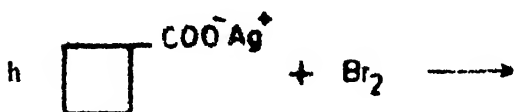
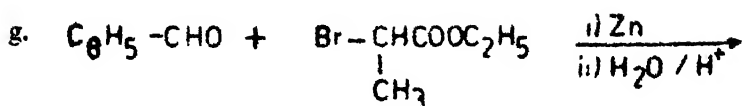
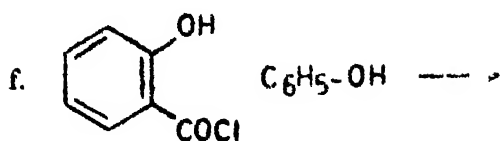


18.4 How will you separate a mixture containing the following components?

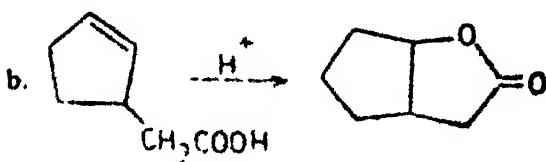
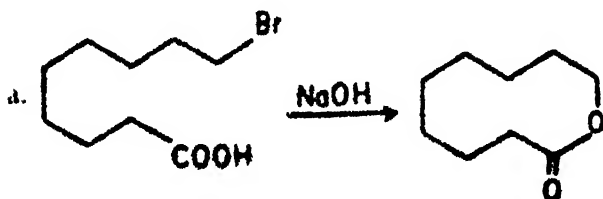


18.5 Predict the products of the following reactions :





18.6 Write mechanisms for the following reactions



18.7 How do you account for the fact that a carboxylic acid does not form an oxime or a phenyl hydrazone?

18.8 Which ketones of the formula $\text{C}_8\text{H}_{16}\text{O}$ will yield an acid by the haloform reaction?

18.9 A hydrocarbon with molecular formula C_8H_{18} yields phthalic acid

as the only product on oxidation. Write the structural formula of the compound.

18.10 Suggest a simple chemical test to distinguish between:

- a. Formic and Acetic acids
- b. Lactic and Malic acids
- c. Crotonic and butyric acids
- d. Acetic acid and acetyl chloride

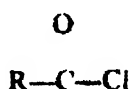
- 18.11 An unknown acid A (mol. wt. 104) contains 34.6% C and 3.85% H. A 3.312 mg sample of the acid requires 7.33 ml of 0.01 N NaOH for complete neutralization. Suggest a structure for the acid.
- 18.12 Describe two methods for the preparation of salicylic acid. How would you convert it into a. phenol b. Salol, c. benzoic acid and d. aspirin? Give its at least two medicinal uses.
- 18.13 How is citric acid prepared? Discuss its important properties. How does it differ from tartaric acid?
- 18.14 a. How is anhydrous formic acid obtained?
b. Describe the mechanism of esterification of an acid.
- 18.15 Give an acceptable explanation for the observation that a carbonyl group in a carboxylic acid does not react with phenyl hydrazine.
- 18.16 Enumerate the general methods for the preparation of aliphatic hydroxy acids and explain how will you proceed to distinguish α , β and γ -hydroxy acids from one another.
- 18.17 On analysis, a monocarboxylic acid was found to contain 40% C, 6.66% H and 53.34% O. 0.985 g of its silver salt gave on ignition 0.54 g of the metal. On treatment with HI, the acid was converted into another acid. The original substance on heating lost water and left a third acid. What is the structural formula of each of the compound referred above?
- 18.18 Why are alcohols weaker than carboxylic acids? Give the structural formulae and IUPAC names of the first five members of monocarboxylic acids and reason out their relative strengths. In what respect does formic acid differ from acetic acid and why?
- 18.19 Give one method of preparation of two properties and one use of anthranilic acid.
- 18.20 Give three general methods for the preparation of saturated aliphatic monocarboxylic acids. Mention their important chemical reactions.
- 18.21 How is lactic acid prepared in the laboratory? What is the action of the following on lactic acid?
a. Acetyl chloride b. dil H_2SO_4 c. Oxidizing agents d. PCl_5

19

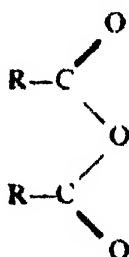
Functional Derivatives of Carboxylic Acids

The carboxyl function, on replacement of the —OH group by other groups, forms a number of important derivatives, among these are.

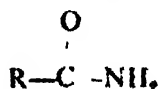
A. Acyl chlorides



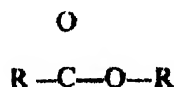
B. Acid anhydrides



C. Acid amides



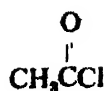
D. Esters



All the above derivatives have a common structural feature, i.e., they possess a carbonyl group and yield an acid on hydrolysis.

Section 4: ACYL HALIDES

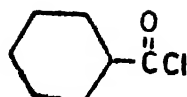
Acyl chlorides do not occur naturally but are prepared in the laboratory as highly reactive starting materials in the formation of other acid derivatives. Both aliphatic and aromatic carboxylic acid chlorides are known. They have both common as well as IUPAC names. The common name is derived by replacing the suffix *-ic* by *-yl* from the name of the parent acid. The name of the halide is added as a second word.



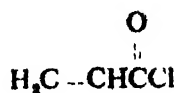
Acetyl chloride



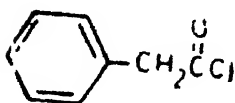
Butyryl bromide



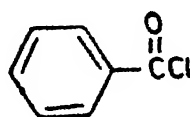
Cyclohexanecarboxylic acid chloride



Propenoyl chloride

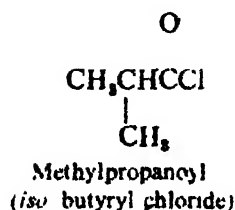
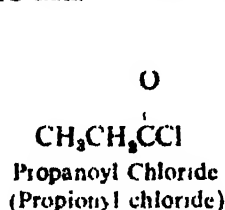


Phenylacetyl chloride



Benzoyl chloride

The IUPAC name is similarly obtained by replacing the suffix *-ic* by *-yl* from the IUPAC name of the acid.



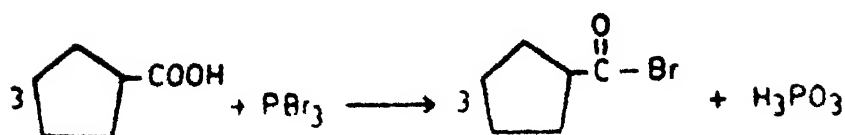
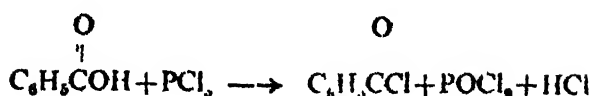
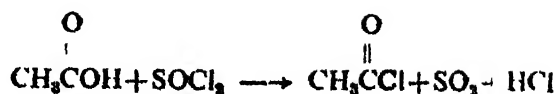
Acid chlorides are corrosive and lachrymatory (i.e. tear producing) compounds. They are polar and react readily with water, alcohol and ammonia. They are incapable of forming H—bond and thus have lower boiling points than their corresponding carboxylic acids.

Table 19.1 Physical Constants of Acyl Chlorides

Compound	Formula	b.p. (°C)
Formyl chloride	HOCl	
Acetyl chloride	CH ₃ COCl	51
Propionyl chloride	CH ₃ CH ₂ COCl	80
Propenoyl chloride	CH ₂ =CHCOCl	73
Benzoyl chloride	C ₆ H ₅ COCl	197

19.1 PREPARATION OF ACYL HALIDES

1. As in the case of the formation of halo compounds from alcohols, the OH group of the carboxyl function is replaced by —Cl or —Br to obtain acyl chlorides or bromides. The most common reagents are phosphorus pentachloride, PCl₅, thionyl chloride, SOCl₂ and phosphorus tribromide, PBr₃.

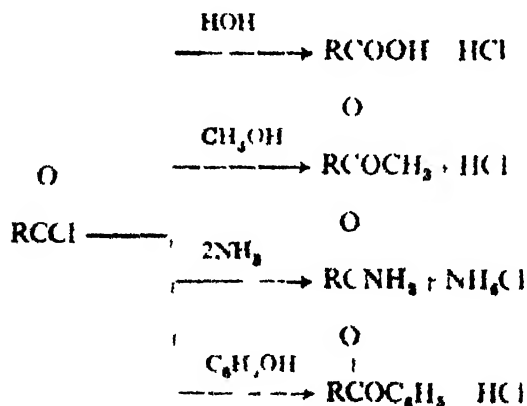
Cyclopentanecarboxylic
acid

Cyclopentanecarboxylic acid bromide

Acyl fluorides, bromides and iodides can also be prepared but they offer no advantage over the less expensive acyl chlorides.

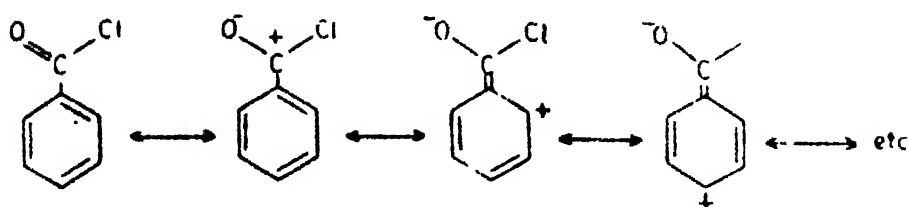
19.2 REACTIONS OF ACYL HALIDES

1. Acyl chlorides may be converted into other acid derivatives as shown below.



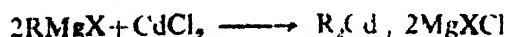
R may be an alkyl or aryl group

Acyl chlorides react rapidly with the above reagents. The reaction, however, with aliphatic acid chlorides is much more vigorous than with the aromatic acid chlorides. In the former the carbonyl carbon atom is a center of low electron density while in the latter this is not so because of resonance with the ring.



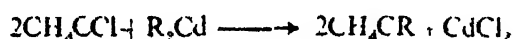
Benzoyl chloride, for instance, is so much less reactive that it can be used as water suspension.

2 Formation of Ketones An alkyl Grignard reagent reacts with anhydrous cadmium chloride, CdCl_2 to form a dialkylcadmium compound, R_2Cd . This intermediate, on reaction with an acyl chloride, yields a ketone

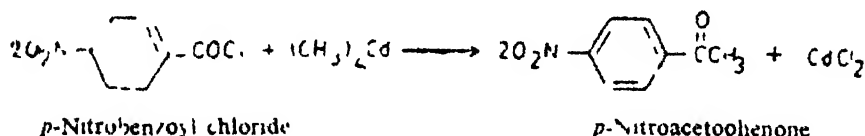


O

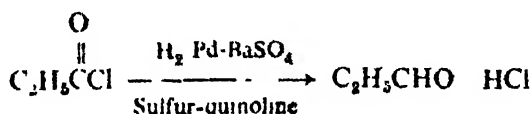
O



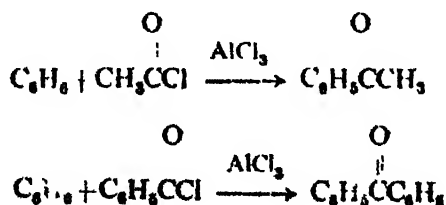
Both aliphatic and aromatic ketones can be prepared in this manner.



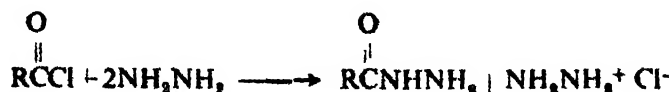
3. Rosenmund Reduction. This reaction requires hydrogen and Pd, which is a catalyst, adsorbed on BaSO_4 , and a catalytic poison like quinoline to slow down the reaction. The result is the formation of an aldehyde.



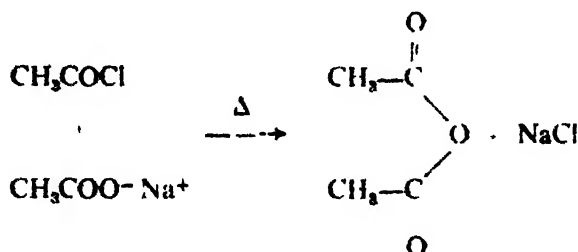
4. Friedel-Crafts Reaction: Preparation of aromatic ketones by the F.C. reaction of acyl chlorides is an important method.



5. *Acid Hydrazides*: Treatment with hydrazine yields acid hydrazides.



6. *Acid Anhydrides*: The acid halide, on heating with the salt of the corresponding acid, yields an anhydride.

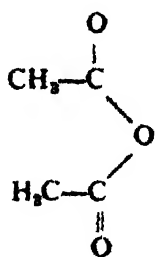


19.3 USES OF ACYL CHLORIDES

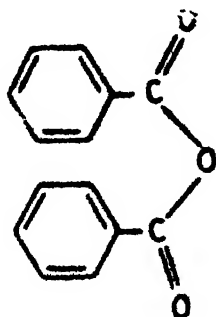
Acyl chlorides are employed as acetylating agents and as starting materials in organic synthesis.

Section B: ACID ANHYDRIDES

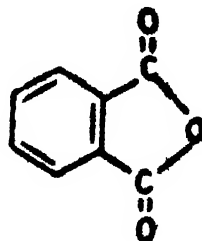
Acid anhydrides are formed by the removal of a molecule of water from two molecules of a carboxylic acid. Most acid anhydrides are symmetrical. Unsymmetrical, or mixed anhydrides are also known but are not much used. Acid anhydrides are also very reactive like the acid chlorides and have penetrating odor. They are useful for synthetic purposes because of their less corrosive action and greater stability. The names of the acid anhydrides are obtained by adding the word anhydride to the name of the corresponding



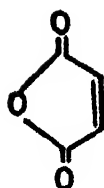
Acetic anhydride



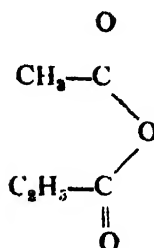
Benzoic anhydride



Phthalic anhydride



Maleic anhydride

Propionic acetic anhydride
(a mixed anhydride)

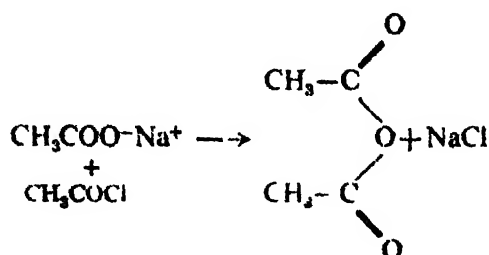
carboxylic acid. Acid anhydrides of aliphatic carboxylic acids are generally liquids whereas those of aromatic acids are solids. They also react with alcohol and ammonia

Table 19.2 Physical Constants of Anhydrides

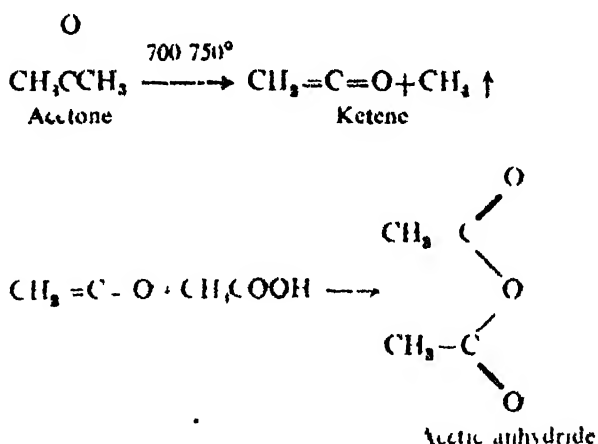
Compound	Formula	m.p. ($^{\circ}\text{C}$)	b.p. ($^{\circ}\text{C}$)
Acetic anhydride	$(\text{CH}_3\text{CO})_2\text{O}$	-73	140
Trifluoroacetic anhydride	$(\text{CF}_3\text{CO})_2\text{O}$		40
Propionic anhydride	$(\text{CH}_3\text{CH}_2\text{CO})_2\text{O}$		169
Succinic anhydride		120	261
Phthalic anhydride		131	284
Benzoinc anhydride	$(\text{C}_6\text{H}_5\text{CO})_2\text{O}$	42	360

19.4 PREPARATION OF ACID ANHYDRIDES

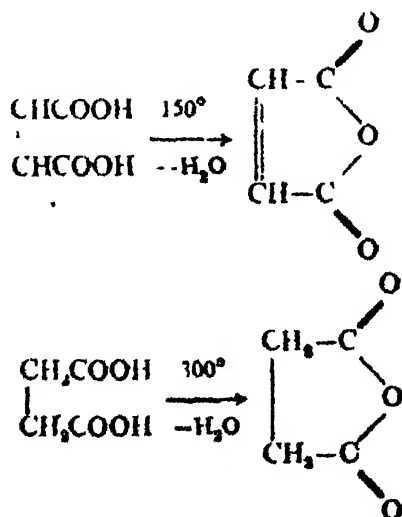
1. Acetic anhydride is obtained by reacting sodium acetate with acetyl chloride:

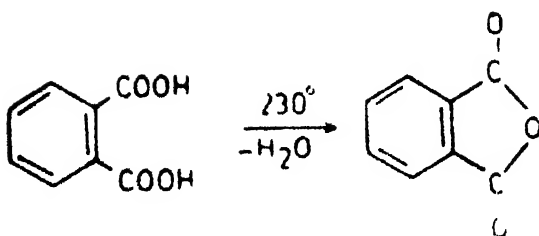


Acetic anhydride is also obtained by the reaction of a ketene, obtained from pyrolysis of acetone, with acetic acid



2. Cyclic anhydrides such as maleic and phthalic anhydrides are prepared by heating the corresponding dicarboxylic acids

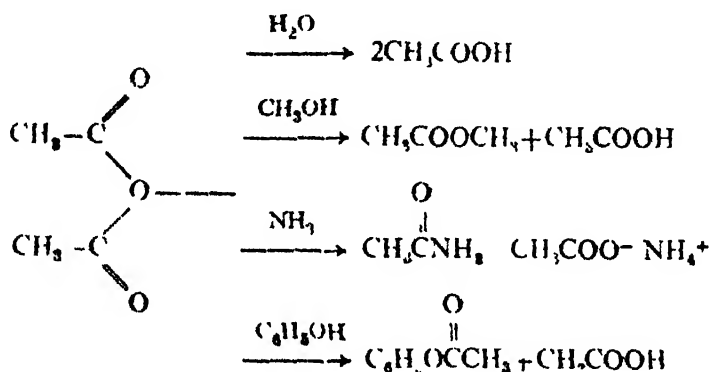




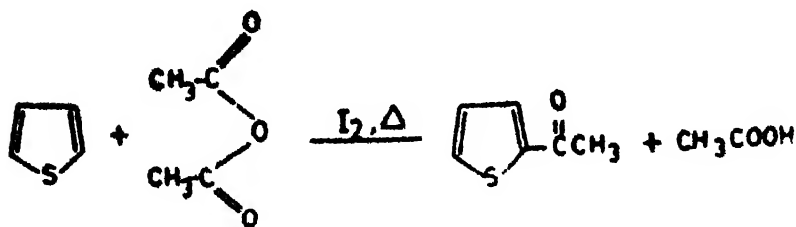
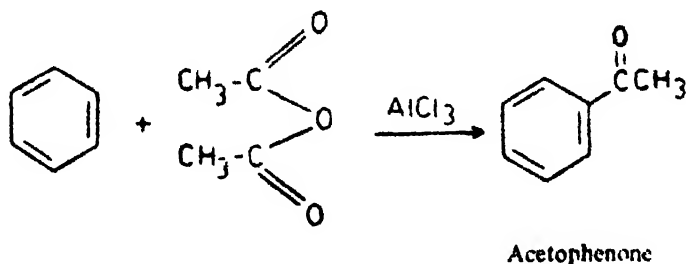
19.5 REACTIONS OF ACID ANHYDRIDES

Acetic anhydride seems to be the only acid anhydride of general importance. It is the source of acetyl groups in the manufacture of rayon and aspirin.

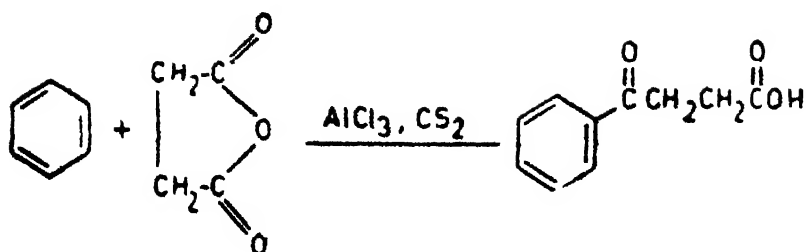
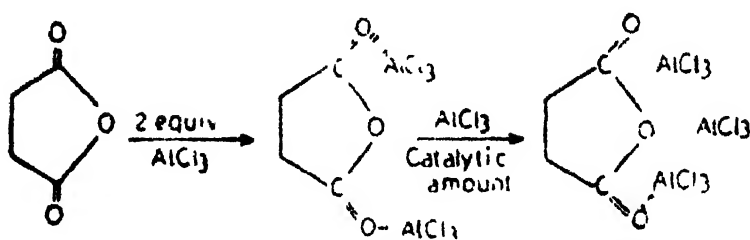
1. Acid anhydrides contain carbonyl groups and thus undergo nucleophilic attack by various electron donors to yield the corresponding products.



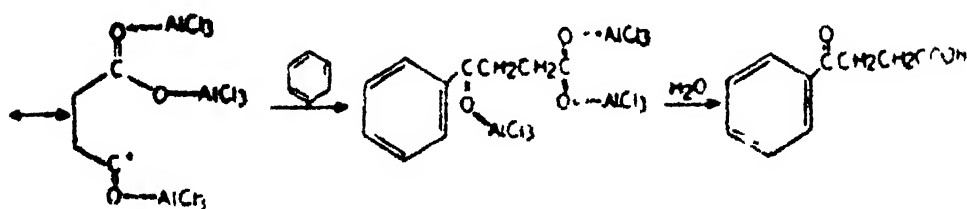
2. Ketones are obtained by the Friedel-Crafts acylation of aromatic hydrocarbons. Acetophenone is formed from acetic anhydride and benzene



Methyl 2-thienyl ketone

 β -Benzoylpropionic acid*Mechanism*

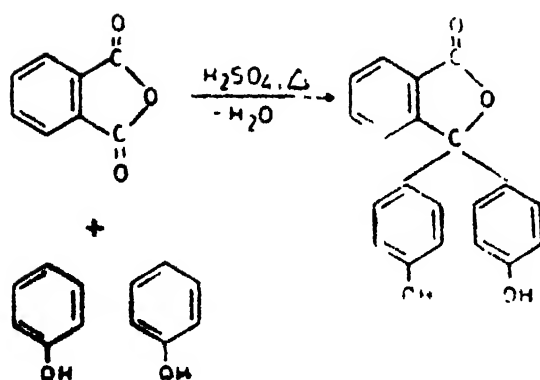
Succinic anhydride

 β -Benzoylpropionic acid

3. Acid anhydrides react with hydroxylamine to yield hydroxamic acid

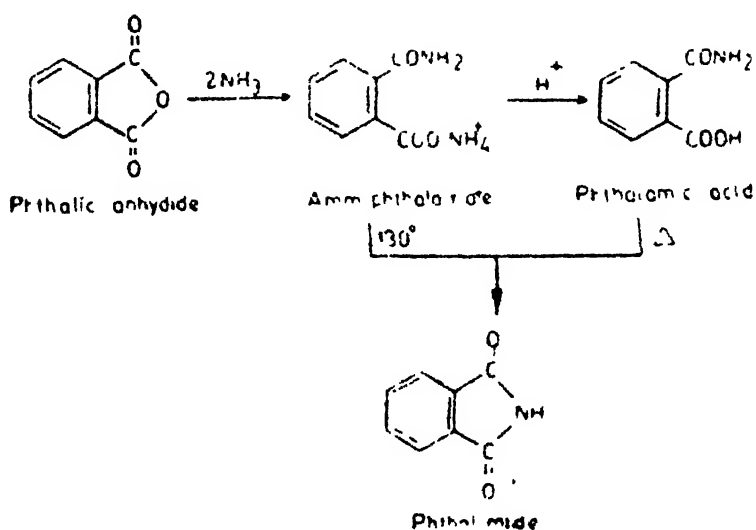


4. Phthalic anhydride condenses with two moles of phenol in the presence of conc. H_2SO_4 to form phenolphthalein.

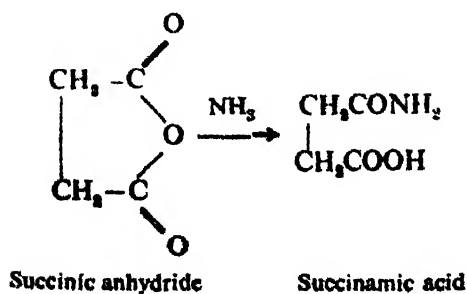


Phenolphthalein

5. Cyclic acid anhydrides react with ammonia to form amides, which on heating lose a molecule of water with the resultant formation of cyclic imides.



6. Succinic anhydride with ammonia forms succinamic acid.

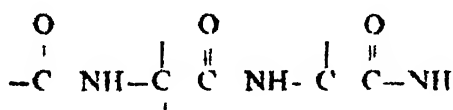


19.6 USES OF ACID ANHYDRIDES

Acetic anhydride is used as an acetylating agent, as a medium in the estimation of alcohols, phenols and in medicines

Section C: AMIDES

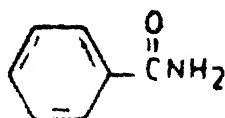
Substances having the structures $R-\overset{\overset{\text{O}}{\parallel}}{\text{C}}-\text{NH}_2$, i.e. in which the hydroxyl group is replaced by an amino group are called amides. Proteins are polymers which contain the amide linkage in the polymer skeleton



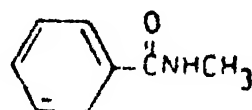
They derive their trivial names by replacing the suffix *-ic* of the parent acid by *-amide* whereas in the IUPAC system they are named as *alkanamides*



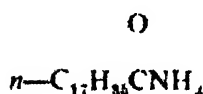
Acetamide
(Ethanimide)



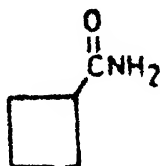
Benzamide



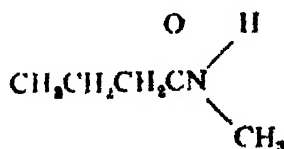
N-Methylbenzamide



Stearamide



Cyclobutane carboxamide



N-Methylbutanamide

Lysergic acid, N, N-diethylamide (LSD) which contains an amide function is a potent hallucinogen

Amides are crystalline solids, often soluble in water. Carboxylic acids are generally identified by making their amide derivatives.

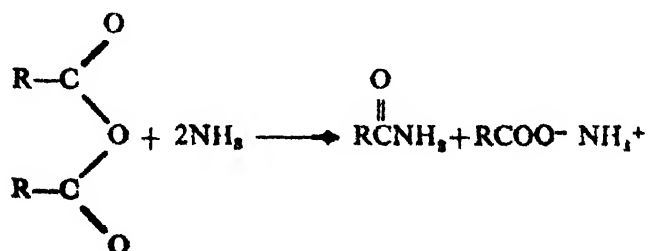
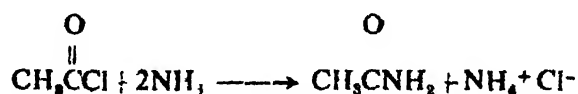
Table 19.3 Physical Constants of Amides

Compound	Formula	b.p. (°C)	m.p. (°C)
Formamide	HCONH_2		3
Acetamide	CH_3CONH_2		82
Propionamide	$\text{CH}_3\text{CH}_2\text{CONH}_2$		79
Benzamide	$\text{C}_6\text{H}_5\text{CONH}_2$		128
Salicylamide	$\text{HO-C}_6\text{H}_4\text{CONH}_2$		139
Phenylacetamide	$\text{C}_6\text{H}_5\text{CH}_2\text{CONH}_2$		154
Oxamide	$\begin{array}{c} \text{O} \quad \text{O} \\ \quad \\ \text{NH}_2\text{C}-\text{CNH}_2 \end{array}$		418
Succinamide	$\begin{array}{c} \text{O} \quad \quad \text{O} \\ \quad \quad \\ \text{H}_2\text{N}-\text{C}-\text{CH}_2-\text{CH}_2-\text{C}-\text{NH}_2 \end{array}$		242
Acetanilide	$\text{CH}_3\text{CONHC}_6\text{H}_5$		114
Benzanilide	$\text{C}_6\text{H}_5\text{CONHC}_6\text{H}_5$		161

19.7 PREPARATION OF AMIDES

Amides are prepared mostly from carboxylic acids and their derivatives

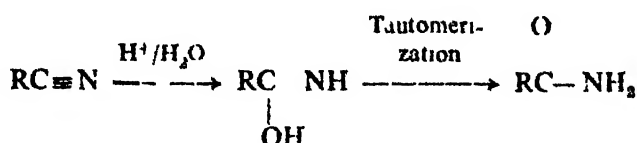
1. Amides can be prepared by the direct action of ammonia on acetyl chloride or anhydride.



2. Ammonium salts of carboxylic acids on heating yield amides.

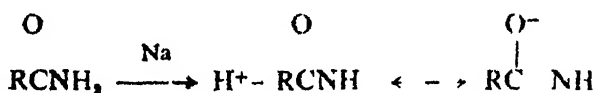


3. Both alkyl- and aryl-nitriles, on partial hydrolysis in an acidic medium, form amides.



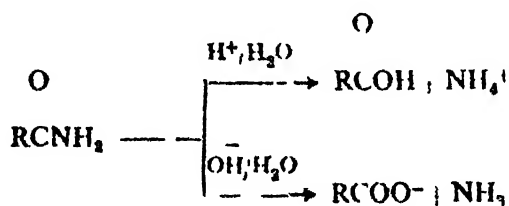
19.8 ACIDITY OF AMIDES

Although amides are considered to be weakly acidic (for instance, K_a for acetamide is $\sim 10^{-15}$), they react with alkali metals to form salts. The reason for the acidity is that the resulting anion can be stabilized by resonance as shown below:



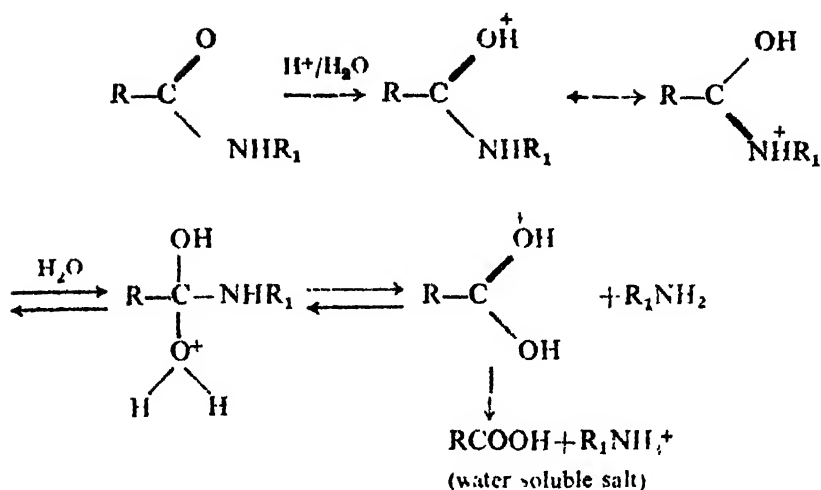
19.9 REACTIONS OF AMIDES

1. Amides may be hydrolyzed in the presence of either an acid or base leading to the formation of the parent acid.

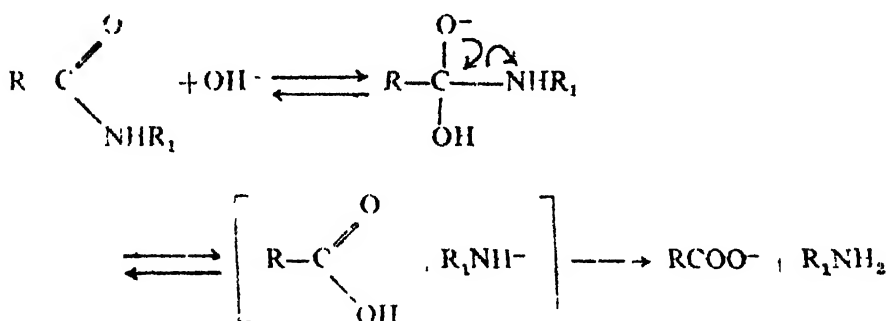


Mechanism

For the acid hydrolysis of an amide the oxygen atom is protonated in contrast to the nitrogen atom because the former is more electronegative and also yields the most stable conjugate acid.

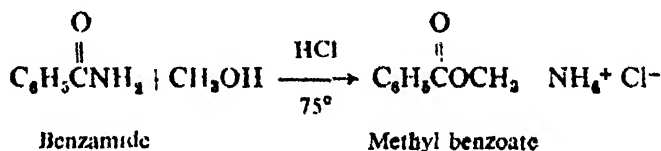


The basic hydrolysis follows the following sequence:

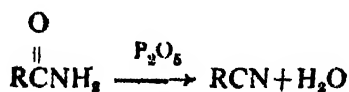


Evolution of ammonia gas on heating an amide in the presence of a base is used as a test for its identification.

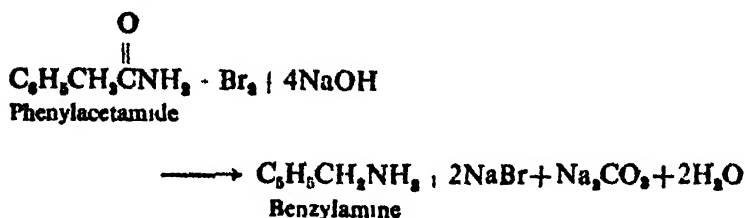
2. Esters are obtained on reacting amides with alcohols in the presence of a mineral acid.



3. Amides lose a molecule of water in the presence of an efficient dehydrating agent such as phosphorus pentoxide to form a nitrile.

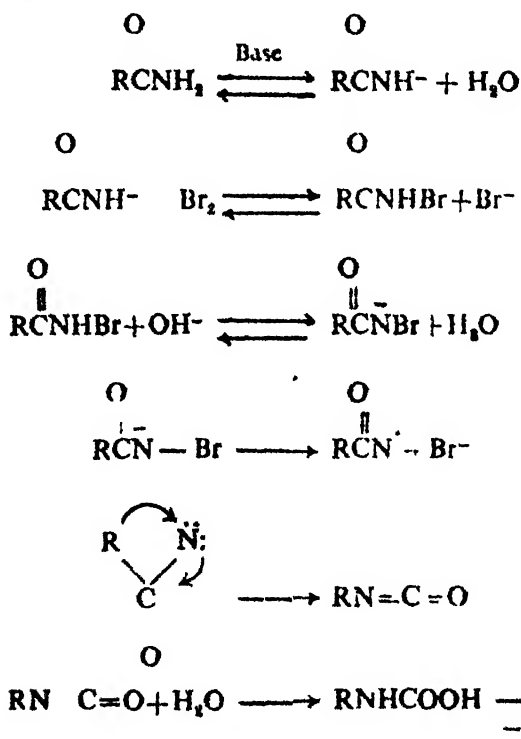


4. *Hofmann Reaction*: A primary amide on treatment with bromine in the presence of an aqueous base forms an amine. The reaction is referred to a *Hofmann Reaction*.



Mechanism

The first two steps are the base-catalyzed bromination of the amide. The N—bromamide is more acidic than the starting amide and forms the corresponding anion. This loses Br^- to form a nitrene. Then a shift of the



alkyl takes group place to yield an isocyanate. This is hydrolyzed to carbamic acid which is easily decarboxylated to an amine.

19.10 UREA

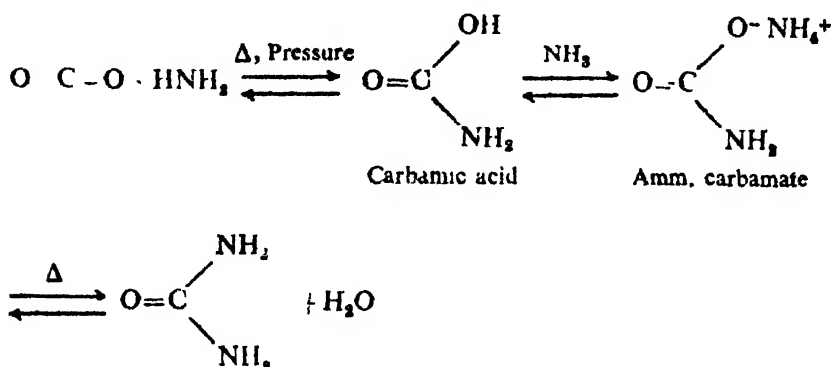
Urea is the diamide of carbonic acid (H_2CO_3). It is excreted in urine as the end-product of protein metabolism. An average adult excretes about 30 g of urea daily. It is an important agricultural fertilizer, also.

Preparation

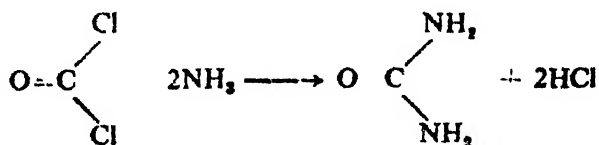
1. Synthesis of urea is of historical importance and was first obtained by Wohler in 1828 by heating ammonium cyanate which gave a blow to the *vital force theory*. The ammonium cyanate, in this case, isomerizes to urea.



2. On a commercial scale urea is prepared by heating a mixture of ammonia and carbon dioxide under pressure.



3. A laboratory preparation of urea includes the reaction between phosgene (COCl_2) and ammonia.

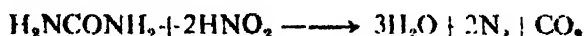


4. Urea may be obtained from urine in a relatively pure state, first by precipitating the phosphates, sulfates, urates and hippurates by adding a solution of barium nitrate followed by barium hydroxide. The precipitates are removed by filtration and the filtrate is concentrated. Urea is extracted with alcohol and decolorized with activated charcoal and finally it is crystallized.

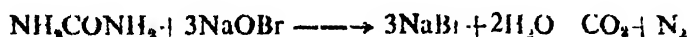
Reactions

1. Urea is weakly basic and forms salts with only strong acids. The fact that it is a stronger base than ordinary amides is due to the fact that the cation is capable of being stabilized by conjugation. With nitric acid urea forms urea nitrate.

6. With cold dil. nitrous acid urea yields nitrogen and carbon dioxide, like other amides on reaction with urea.



7. Alkaline solution of hypobromite also liberates nitrogen and carbon dioxide.



USES OF UREA

Urea is used as a fertilizer, in the preparation of barbiturates, and in the formation of urea-formaldehyde resin

Section D: ESTERS

Esters probably constitute the most important class of carboxylic acid derivatives. They occur widely in nature and are responsible for the fragrance of many fruits and flowers, for example:

Ethyl formate - Artificial rum flavor

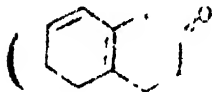
n-Amyl acetate - Pears

iso-Amyl acetate - Bananas

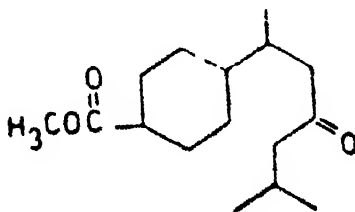
n-Amyl butyrate - Apricots

Octyl acetate - Oranges

The odor of newly mown hay or sweet clover is due to coumarin

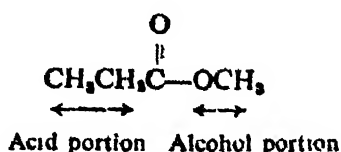
() , a cyclic ester (lactone of *ortho*-hydroxycinnamic acid).

Several other types of artificial flavors such as strawberry, apples, cherry, raspberry, etc. are made chiefly from mixtures of esters. Another interesting example of naturally occurring ester is that of *juvabione*, it is an insecticide and is specific for certain types of insects.

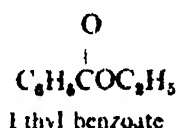
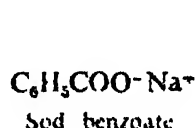
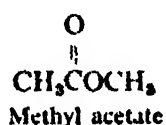
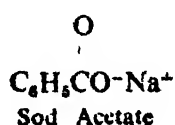


Juvabione

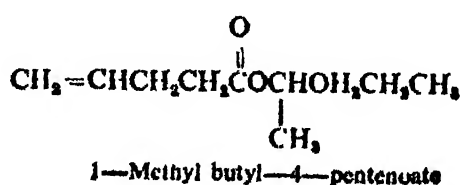
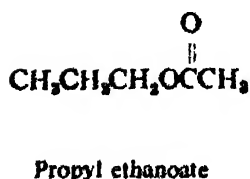
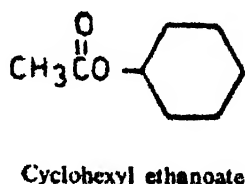
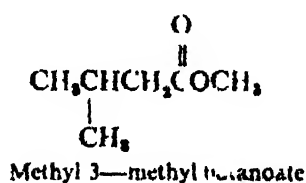
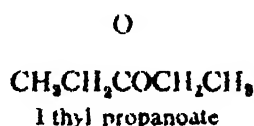
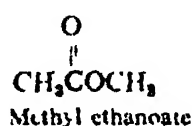
Esters are formed by replacement of the hydroxy group of the acids by an alkoxy group, i.e., from a reaction between an acid and alcohol.

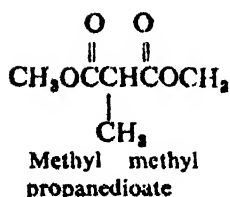


Esters may be named both in the trivial as well as IUPAC system of nomenclatures. In the trivial nomenclature the esters are named in the same manner as acid salts except that the alkyl part of the alcohol is used in place of the metal, as illustrated below:



In the IUPAC system the acid chain is used as the stem in naming the ester. The suffix *-ate* is used in place of *-ic* of the acid. It is necessary to number the substituent on the chain. The first part of the name is derived from the alkyl group of the corresponding alcohol





The alkyl derivatives of the non-existent *ortho* forms of carboxylic acids

with the general formula $\left(\text{R}-\text{C} \begin{array}{l} \text{OH} \\ \text{OH} \end{array} \right)$ are called *ortho* acids, the corres-

ponding ester, for instance, $\text{H}-\text{C} \begin{array}{l} \text{OCH}_3 \\ \text{OCH}_3 \end{array}$ is called *ortho*-formic ester.

Ortho-phosphoric acids $\left(\text{HO}-\text{P} \begin{array}{c} \text{O} \\ \uparrow \\ \text{OH} \end{array} \right)$ are fairly stable in most cases

but the *ortho* forms of organic acids lose water so readily that they are known only in the form of their esters or other derivatives. Esters are mostly liquids and possess a pleasant smell. Their boiling points are lower than the carboxylic acids of comparable molecular weights.

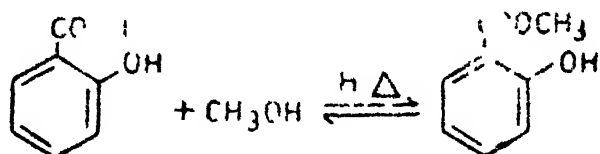
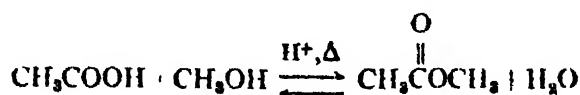
Table 19.4 Physical Constants of Esters

Compound	Formula	b.p. (°C)
Ethyl formate	HCOOC_2H_5	54
Methyl acetate	$\text{CH}_3\text{COOCH}_3$	58
Ethyl acetate	$\text{CH}_3\text{COOC}_2\text{H}_5$	77
<i>n</i> -Propyl acetate	$\text{CH}_3\text{COOC}_3\text{H}_7$	102
Ethyl propionate	$\text{C}_2\text{H}_5\text{COOC}_2\text{H}_5$	99
Ethyl benzoate	$\text{C}_6\text{H}_5\text{COOC}_2\text{H}_5$	213
Benzyl acetate	$\text{CH}_3\text{COOCH}_2\text{C}_6\text{H}_5$	214

19.11 PREPARATION OF ESTERS

The following general methods may be used to prepare esters.

1. **Esterification of Carboxylic Acids:** A direct reaction between a carboxylic acid and alcohol under the catalytic effect of sulfuric acid yields an ester. This is a reversible reaction and is known as the *Fischer esterification*.



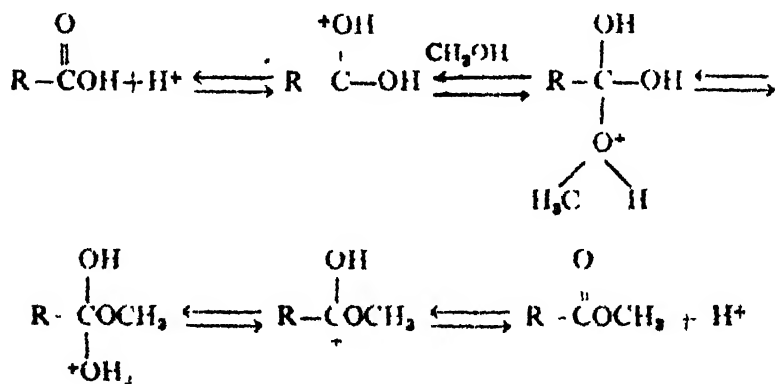
Salicylic acid

Methyl salicylate

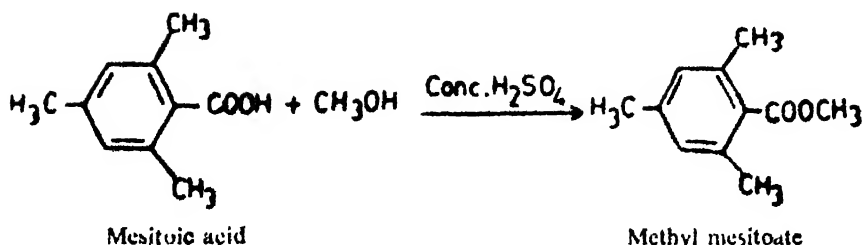
The disadvantage of this method is that the equilibrium is reached slowly and yield of the ester is low.

Mechanism

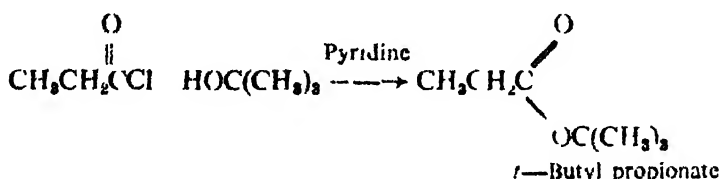
A preliminary protonation of the oxygen of the carbonyl takes place followed by the nucleophilic attack of an alcohol molecule to form a tetrahedral intermediate. Then a proton transfer and loss of a water molecule forms an intermediate which loses a proton and yields the ester.



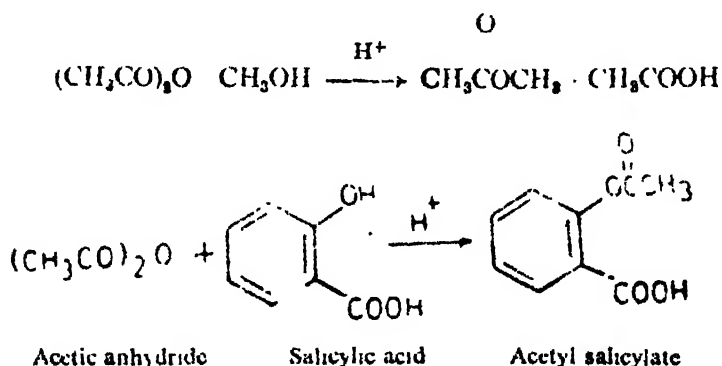
A secondary alcohol may be used similarly, a tertiary alcohol dehydrates readily in the presence of a mineral acid whereas phenols react very slowly. To prepare an ester from a tertiary alcohol or a phenol, the acid chloride is refluxed with alcohol along with an organic base, usually N, N-dimethylaniline. Sterically hindered acids require more drastic conditions for esterification. Mesitoic acid is esterified with CH_3OH in the presence of conc. H_2SO_4 .



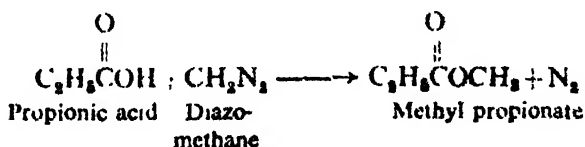
2. *From Acid Chlorides and Anhydrides:* As stated above, esters of tertiary alcohols are prepared by the use of an acid chloride and a tertiary alcohol.



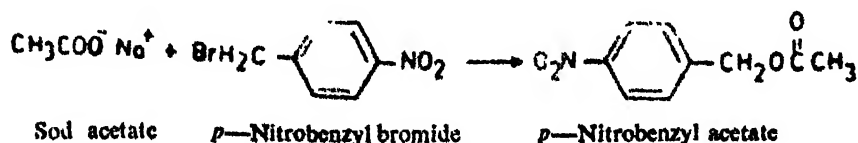
Acid anhydrides on reaction with alcohols or phenols in the presence of acid form esters.



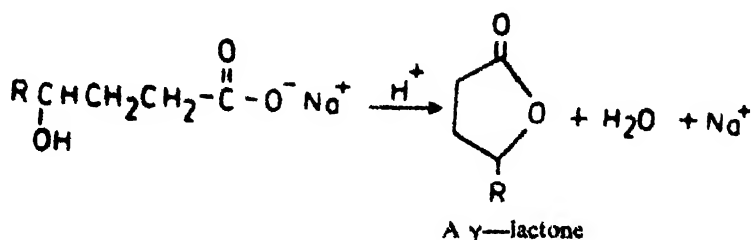
3. Reaction of a carboxylic acid with diazomethane provides a good laboratory method for the preparation of esters.



4. Another method to prepare esters is the reaction between the salt of a carboxylic acid with an alkyl halide.

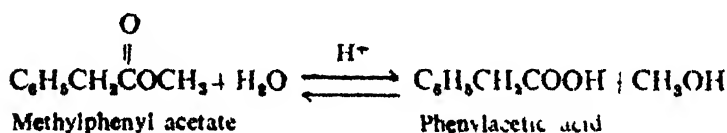
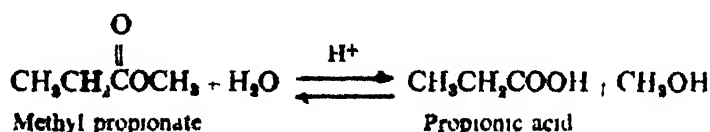


5. Cyclic esters may be obtained by intramolecular esterification of hydroxy acids.



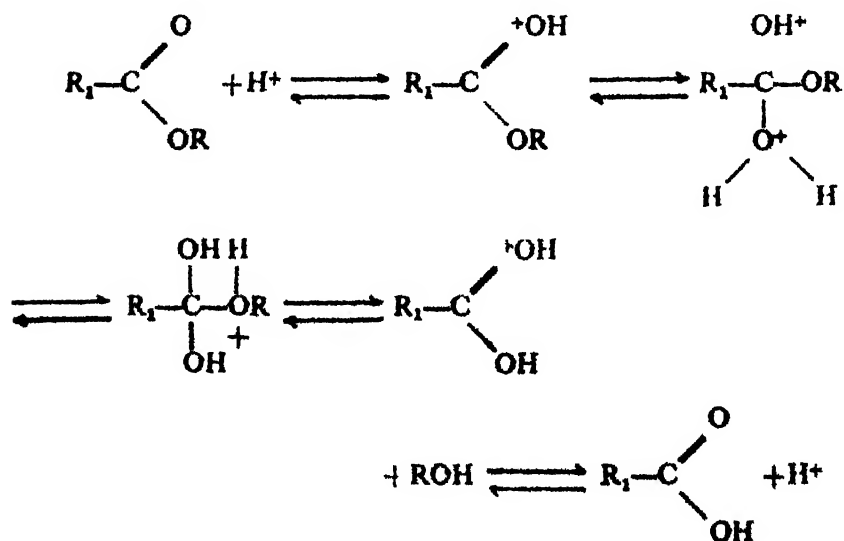
19.12 REACTIONS OF ESTERS

1 *Hydrolysis* Hydrolysis of an ester to give a carboxylic acid and an alcohol is also catalyzed by strong mineral acids. The reaction is just the reverse of the esterification reaction

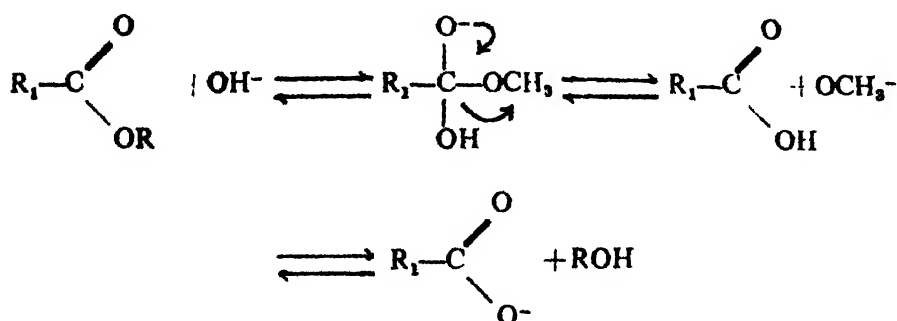


Mechanism

The mechanism of hydrolysis requires protonation of the ester, addition of water, proton transfer and elimination of alcohol

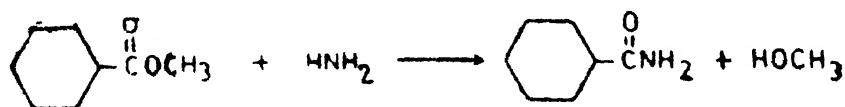


This mechanism also illustrates the principle of microscopic reversibility. The hydrolysis may also be accomplished with an aqueous base and the process is known as *saponification* (Latin, *sapon*, soap). The mechanism involves the following sequence of reactions:



The hydroxyl ion being a strong nucleophile adds to the carbonyl carbon to form a tetrahedral intermediate. Then a methoxide ion is lost and a rapid acid—base reaction takes place to give a carboxylate ion.

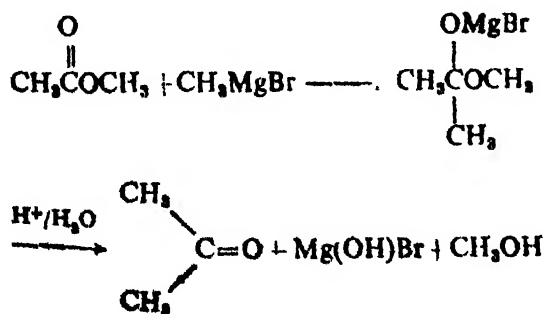
2. *Aminolysis*: Ammonia, like water, also cleaves the ester linkage to form an amide



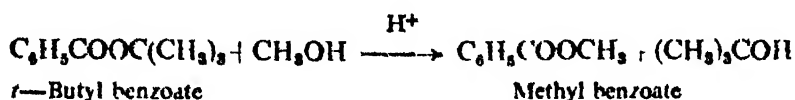
Cyclohexyl carboxamide

Amines react similarly to form substituted amides, for example, methyl *m*-toluate and diethylamine form *N*, *N*-diethyl *m*-toluamide—an insect repellent.

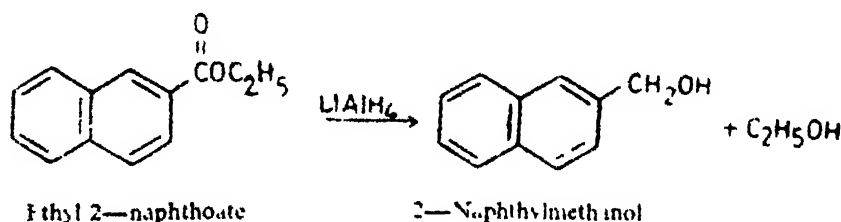
3. *Reaction with Grignard Reagents*: A Grignard reagent adds to the carbonyl group of an ester as it does with an aldehyde or ketone. The adduct decomposes to a ketone. The ketone, however, cannot be isolated it being very reactive and so reacts further to form a tertiary alcohol.



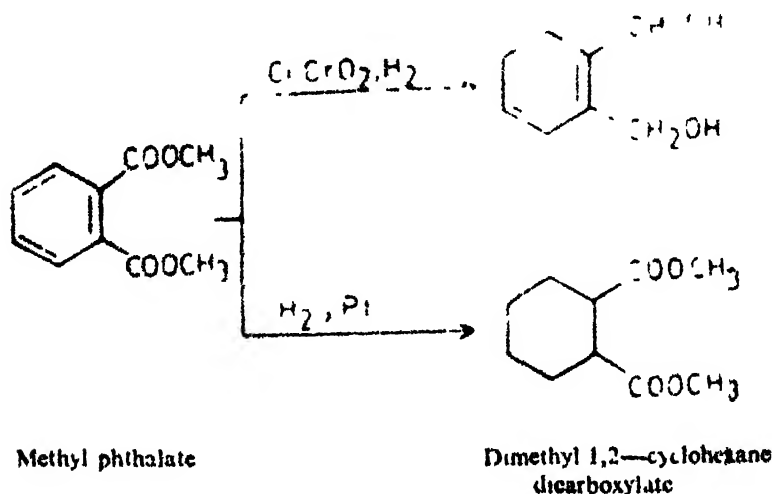
4. *Transesterification*: Treatment of an ester with an alcohol different from that used in the preparation of the ester itself may cause an ester exchange to take place. This process is known as *transesterification*. The reaction is catalyzed by mineral acids



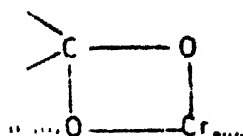
5. *Reduction*: Esters can be reduced by lithium aluminum hydride in a manner similar to carboxylic acid. The process results in the formation of two alcohols and is known as *hydrogenolysis*.



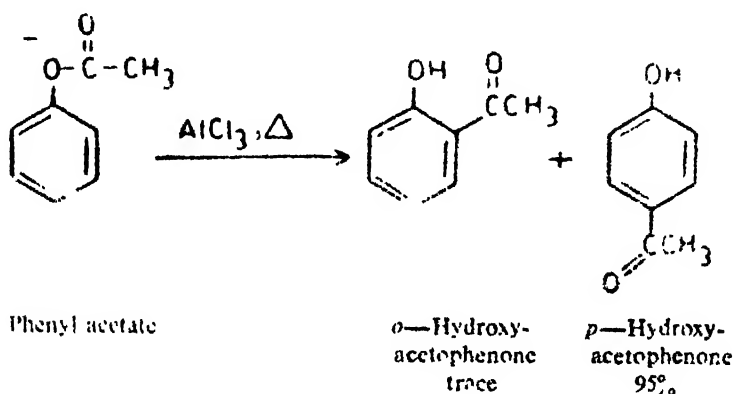
Though LiAlH_4 is not selective in such reactions, another reagent called copper chromium oxide (CuCrO_2) is used for selective reduction of the carboxylic group.



The selectivity of the reagent possibly arises from the strong absorption of the polar group on the surface of the metal oxide as indicated below:



6. *Fries Rearrangement*: Aromatic esters under the action of aluminum chloride as catalyst give hydroxy ketones.



7. With hydrazine, esters form hydrazides.

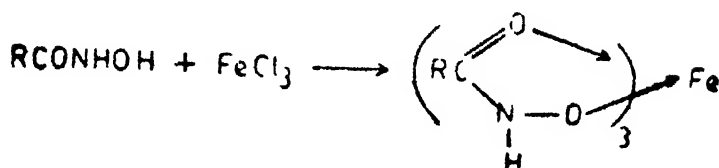
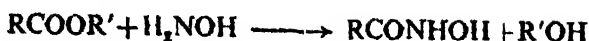


19.13 USES OF ESTERS

Esters are extensively used as artificial flavoring agents and as solvents for resins and as plasticizers.

19.14 DETECTION OF ESTERS

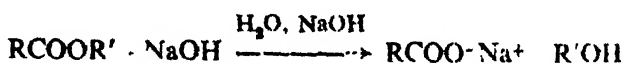
An ester function in an unknown sample may be identified by the hydroxamic ester test. In this test, a small quantity of the ester and hydroxylamine hydrochloride in ethanol is heated with sodium hydroxide solution. The mixture is acidified followed by the addition of 1–2 drops of FeCl_3 solution. Development of a red-violet color indicates the presence of an ester. The chemical reaction involved is the following:



Ferric hydroxamate

Acid chlorides, anhydrides and amides also respond to this test.

A satisfactory identification, however, involves the hydrolysis of the ester and the preparation of derivatives of both the acid and the alcohol fragments. The hydrolysis is accomplished in the presence of an aqueous base.



This procedure may be carried out quantitatively and the resulting *saponification equivalent* is equal to the equivalent weight of the ester. It is defined as the weight of the ester, in grams, which reacts with one gram equivalent of a strong base. For this purpose, a known weight of the ester is hydrolyzed in the presence of an excess base of known strength and the unreacted base is titrated against a standard acid using phenolphthalein indicator. The saponification equivalent is then calculated as follows:

$$\text{Saponification equivalent} = \frac{\text{mg of ester}}{\left(\frac{V_1}{N_1} \right)_{\text{Base}} - \left(\frac{V_2}{N_2} \right)_{\text{Acid}}}$$

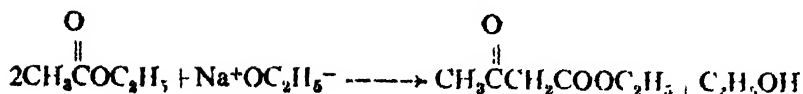
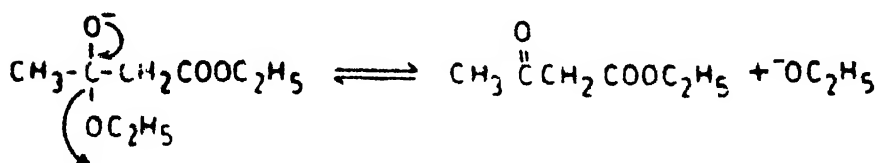
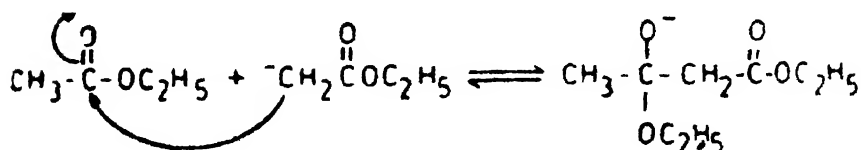
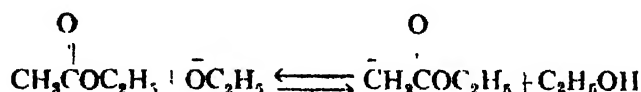
For an ester of a monobasic acid, the value is equal to the molecular weight and for a dibasic acid ester it is one half the molecular weight of the ester.

Section E: ESTERS OF SPECIAL INTEREST

Two esters, namely acetoacetic ester $\text{CH}_3\text{CCH}_2\text{COOC}_2\text{H}_5$ and malonic ester $\text{CH}_2(\text{COOC}_2\text{H}_5)_2$ have found considerable utility in organic synthesis. These can be prepared in good yields from commercially available starting materials.

19.15 ACETOACETIC ESTER

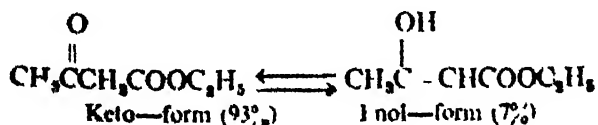
Acetoacetic ester or ethyl acetoacetate is obtained by the self-condensation of ethyl acetate in the presence of excess sodium ethoxide. The process is known as *Claisen ester condensation*.

*Mechanism*

The mechanism is similar to the aldol condensation. Ethoxide ion being a strong base abstracts a proton from the ester molecule to form a resonance stabilized enolate anion. This ion makes a nucleophilic attack subsequently on the carbonyl carbon atom of a second molecule of the ester. Then a subsequent ejection of the ethoxide ion leads to the product. Acetoacetic ester is converted to its enolate ion in the presence of excess base. The ester is obtained by acidification.

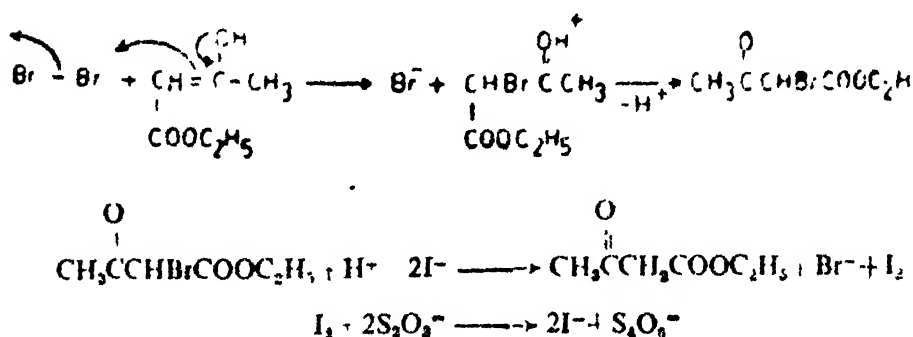
If this reaction is carried out with a mixture of two different esters bearing α -hydrogen then as expected a mixture of four products is obtained as in the aldol condensation. The reaction is thus rendered useless for synthetic purposes under these conditions. However, the product of self-condensation of only one ester finds large synthetic applications in organic chemistry for conversion into higher aldehydes, ketones and carboxylic acids. This is detailed on page 509.

Acetoacetic ester displays the phenomenon of *keto-enol tautomerism*. One form is characterized by the presence of a keto group while the other one is characterized by the presence of an enol.



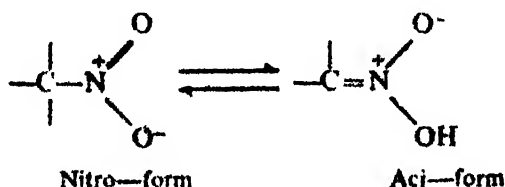
Such compounds normally do not exist as keto compounds or enol compounds under ordinary conditions, rather a mixture of the two. Qualitatively it has been observed that the keto form condenses with 2, 4—dinitrophenylhydrazine and the enol-form gives a color test with FeCl_3 . The enol-form is, however, less important because of its instability, but it is involved in many reactions of aldehydes and ketones. The constitutional isomers are called *tautomers* and this phenomenon is given the name *tautomerism*. Acetoacetic ester is an example of keto—enol tautomerism. The tautomers are different compounds unlike resonance structures which are different attempts to show the bonding in a single compound.

In many cases it may not be possible to isolate the two tautomers because one being more stable than the other. Their existence, nevertheless has been indicated by chemical tests, refractive index and spectral analysis. Quantitatively each form of the tautomeric equilibrium can be measured by a chemical method. This necessitates the reaction of bromine to a known amount of the ester in ethanol. The enol—form reacts at a faster rate than the keto-form. Then β —naphthol is added to remove excess bromine followed by potassium iodide solution and hydrochloric acid and the liberated iodine is titrated with a standard sodium thiosulfate solution.



The enolization is subject to both acid and base catalysts. The keto—form is favored in basic solution.

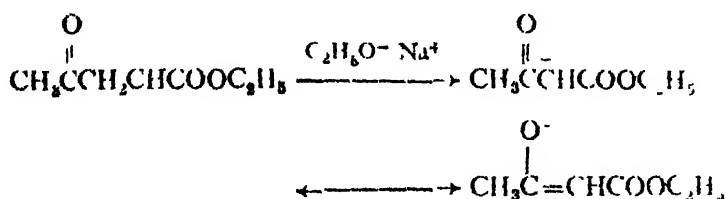
Nitroalkanes similarly exhibit tautomerism. The tautomeric forms of the nitro compound is known as the aci—form. The nitro form is the more stable.



SYNTHETIC USES OF ACETOACETIC ESTER

Acetoacetic ester contains an active methylene group. The hydrogen atoms attached to a saturated carbon atom which has one or more electron

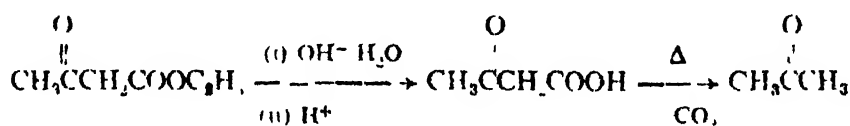
attracting group such as >C=O , $-\text{NO}_2$, $-\text{COOC}_2\text{H}_5$, $-\text{CN}$, etc., linked to it are acidic and can be abstracted by a base to form a carbanion



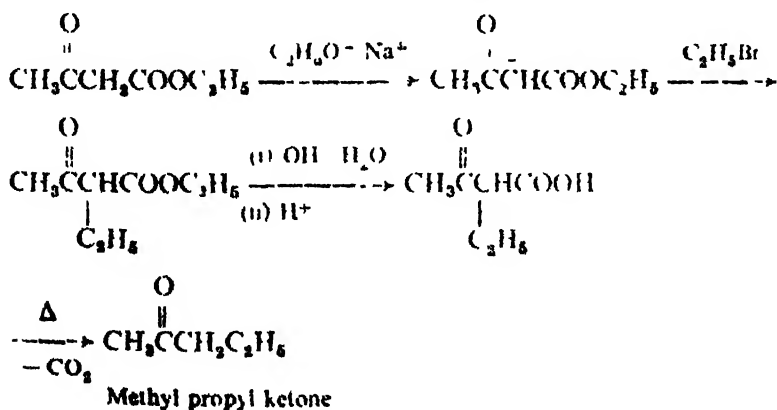
The acidic group, i.e. $-\text{CH}_2$ is called an *active methylene group* and all such compounds containing this group are called active methylene compounds. This property of acetoacetic ester and its condensation with other reagents leads to important products.

1. Synthesis of Ketones

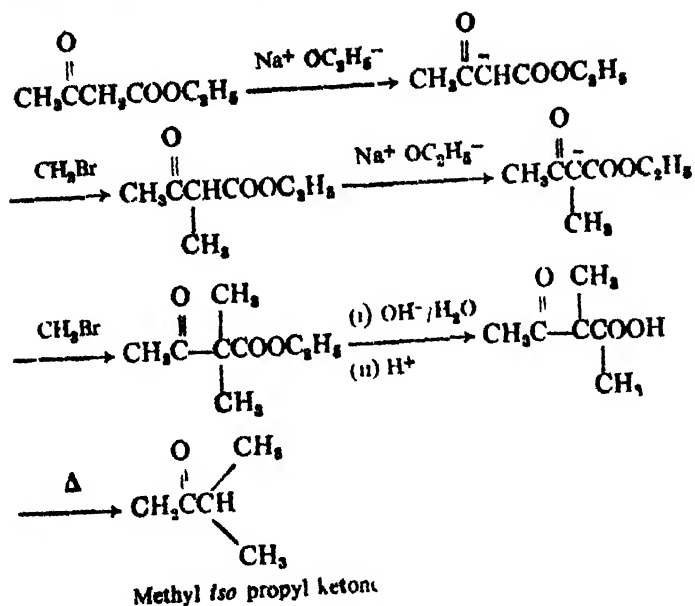
a. Acetone is obtained by the direct hydrolysis of the ester and subsequent decarboxylation of the resultant acid



b. Preparation of substituted ketones from acetoacetic ester constitutes a valuable method for their preparation. The ester is treated with sodium ethoxide to give the sodium derivative which is then reacted with an alkyl halide leading to the formation of an alkyl derivative of the ester. Subsequent alkaline hydrolysis and decarboxylation of the acid yields the ketone.

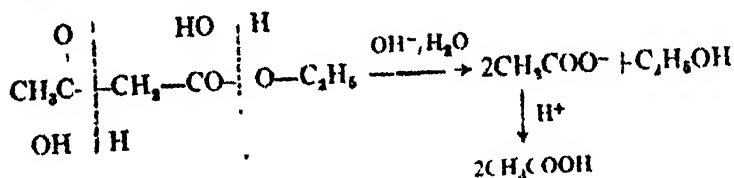


If desired, both the hydrogen atoms of the methylene group can be replaced by alkyl groups and then subsequent treatment as above yields a distributed ketone.

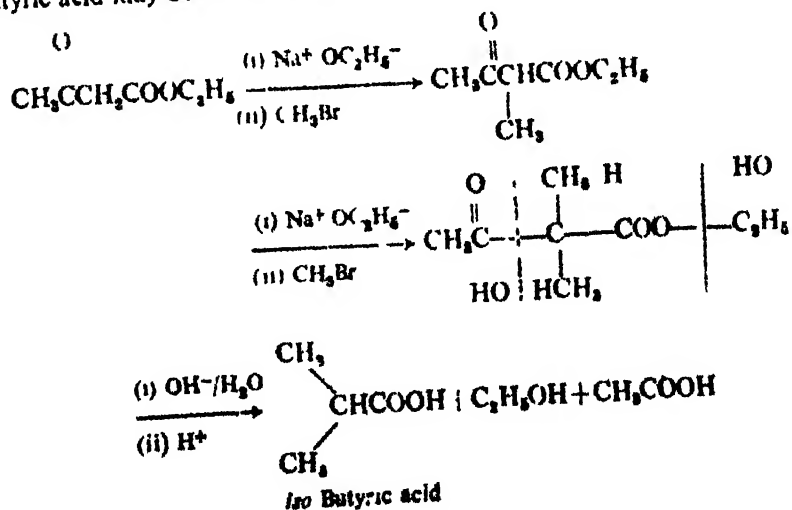


2. Synthesis of Monocarboxylic Acids

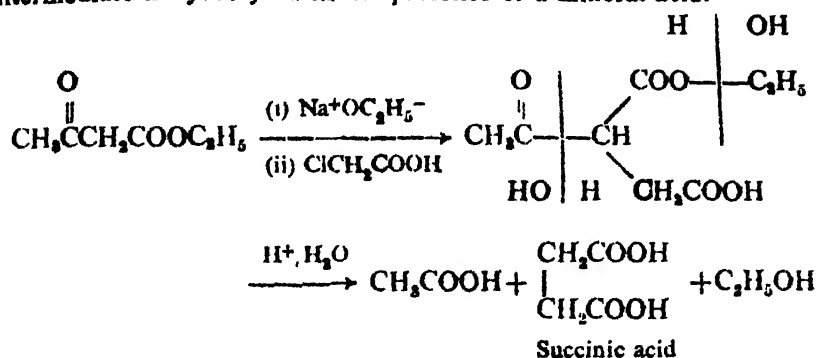
a. Direct hydrolysis of the ester leads to two molecules of acetic acid



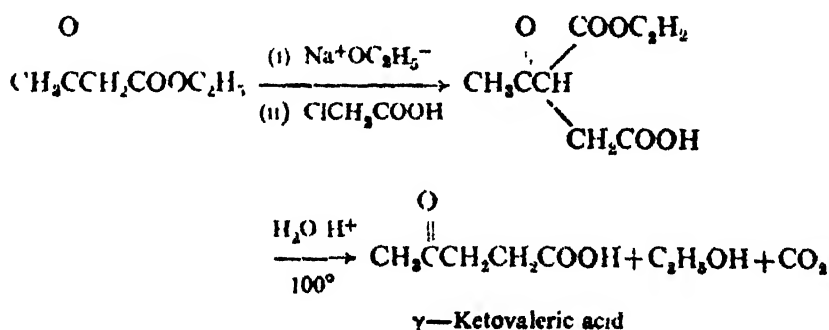
b. A higher acid may be obtained in the manner discussed above. isobutyric acid may be obtained as follows



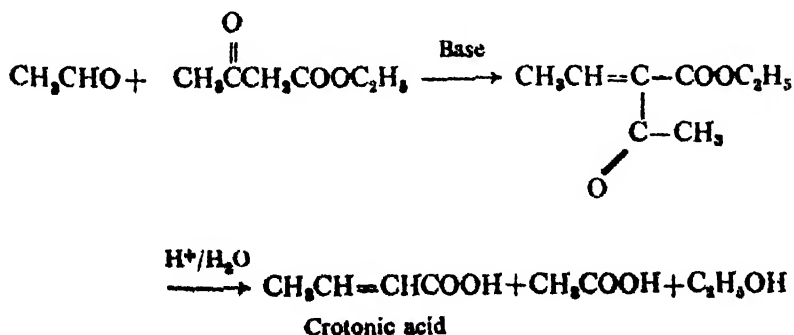
3. *Synthesis of Dicarboxylic Acids*: The ester is first converted into its sod. derivative and then reacted with a chloro carboxylic acid. The transient intermediate is hydrolyzed in the presence of a mineral acid.



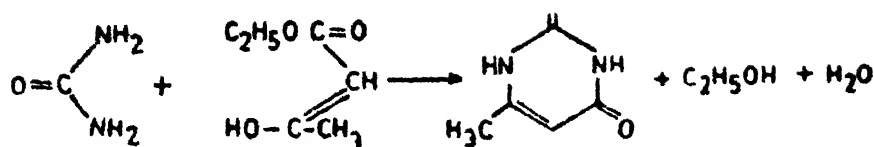
4. *Synthesis of Keto Acids*: The sod. derivative of the ester is condensed with a halo acid and subsequently hydrolyzed and decarboxylated to obtain a keto acid.



5. *Synthesis of α, β -Unsaturated Acids*: The ester is condensed with acetaldehyde and the resultant product is hydrolyzed,

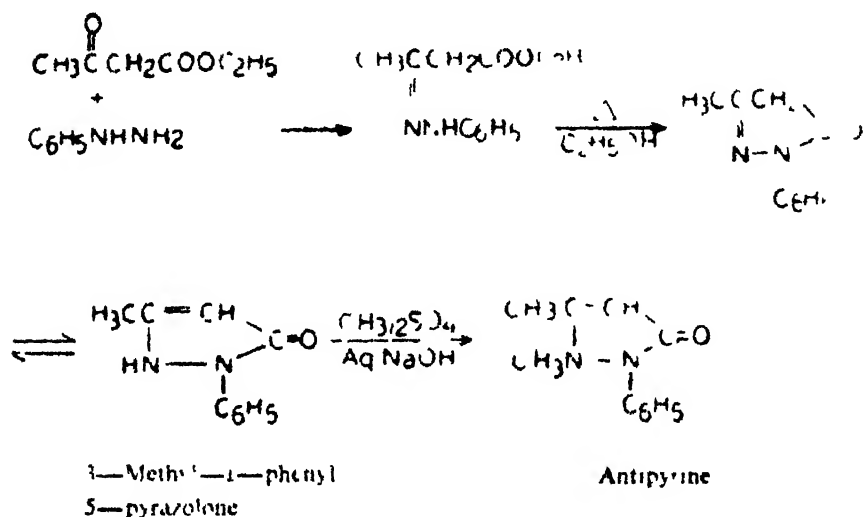


6. *Synthesis of Heterocyclic Compounds*: One mole of the ester condenses with one mole of urea to form 4-methyluracil which is used as a sedative.



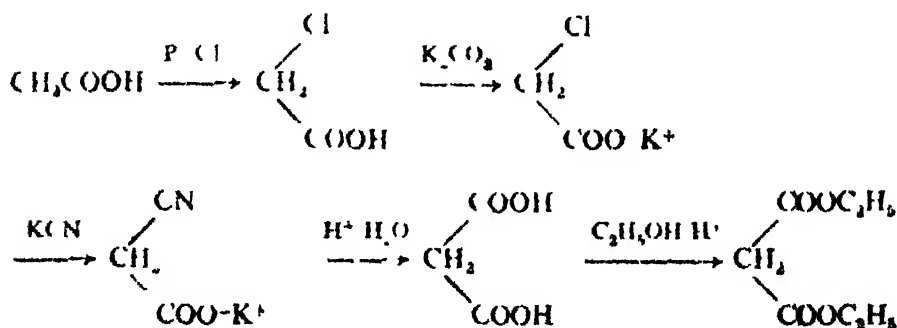
4-Methyl uricil

7. *Synthesis of Antipyrine* The antipyretic drug, antipyrine or phenazone, is obtained by the following sequence



19.16 MALONIC ESTER

Diethyl malonate or malonic ester may be prepared starting from acetic acid according to the following sequence of reactions

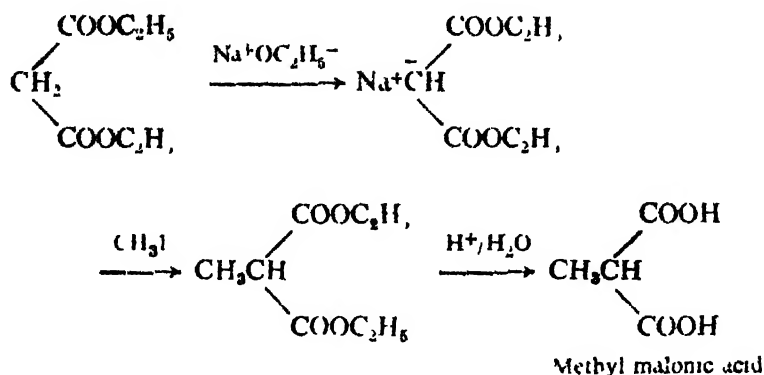


Chloroacetic acid is converted into its potassium salt and then reacted with KCN to yield a nitrile. Acidic hydrolysis of the nitrile and subsequent esterification gives malonic ester.

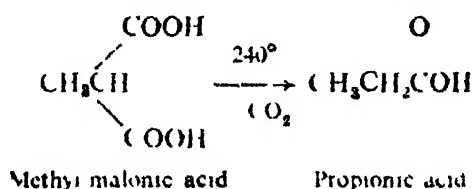
This ester also contains an active methylene group and is a useful intermediate for several organic synthesis.

Synthetic Uses

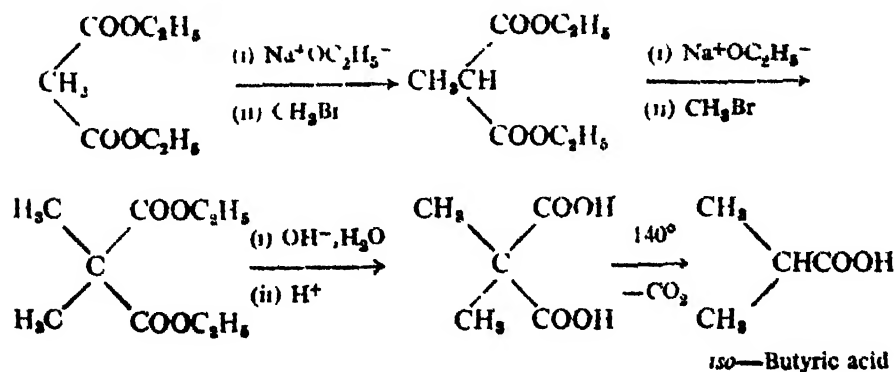
1. **Synthesis of Substituted Derivatives of Malonic Acids:** The sod. malonic ester is treated with an appropriate alkyl halide and subsequently hydrolyzed.



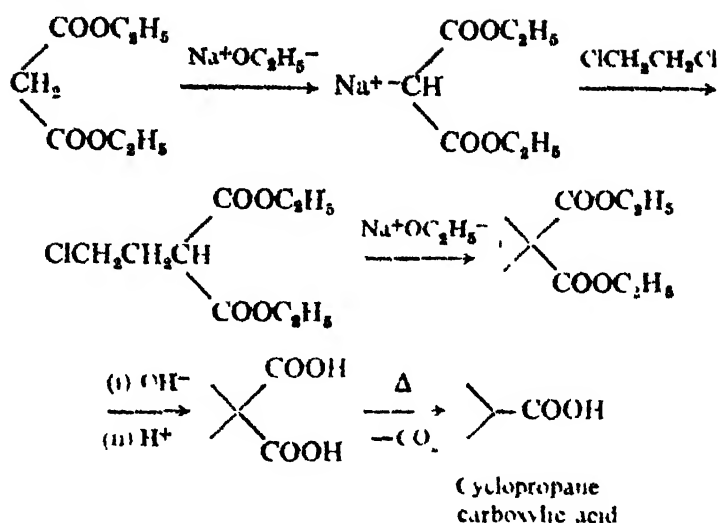
2. **Synthesis of Monocarboxylic Acid:** A monocarboxylic acid may be obtained by the decarboxylation of the acid obtained above.



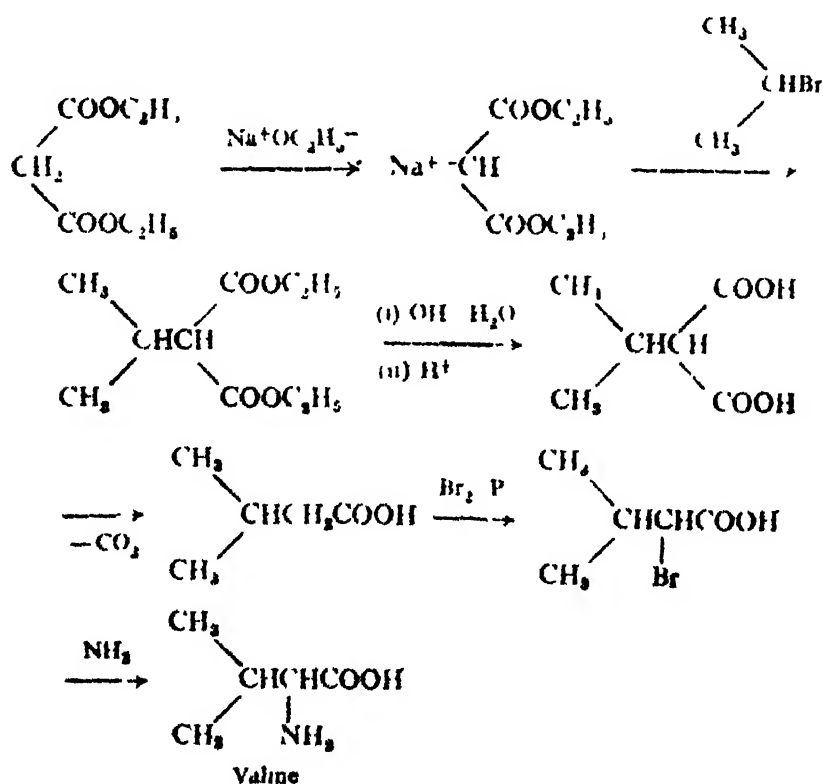
3. **Dialkyl Monocarboxylic Acids:** Both the hydrogen atoms of the active methylene group are replaced by alkyl groups and then hydrolyzed. *iso*-Butyric acid, thus, can be prepared as follows:



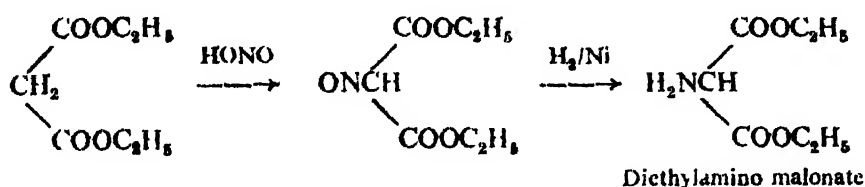
4. **Synthesis of Cyclic Acids:** If a suitable dihalide is employed, then the malonic ester can be added at the ends of the halide to form a cyclic ester. Subsequent hydrolysis yields a cyclic acid.



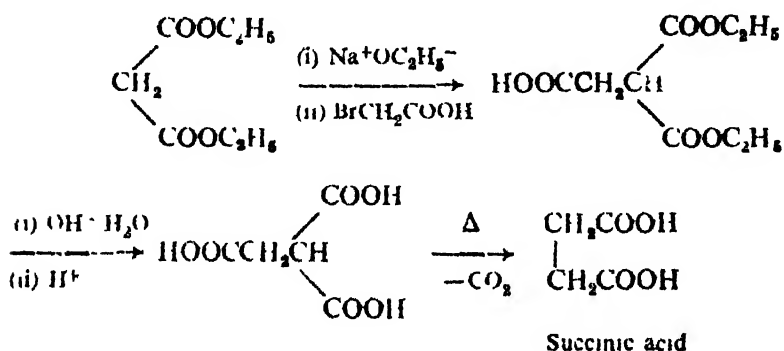
5. *Synthesis of α -Amino Acids* : The sodium derivative of the ester is condensed with an alkyl halide and a monocarboxylic acid is obtained first on hydrolysis. It is then brominated at the α -position according to the Hell-Volhard-Zelinsky method and then treated with ammonia to obtain an α -amino acid



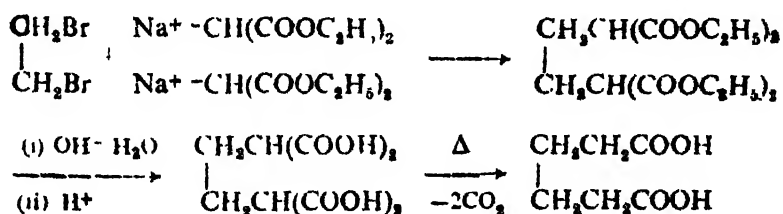
6. *Formation of Diethylamino Malonate*: It is formed according to the following scheme:



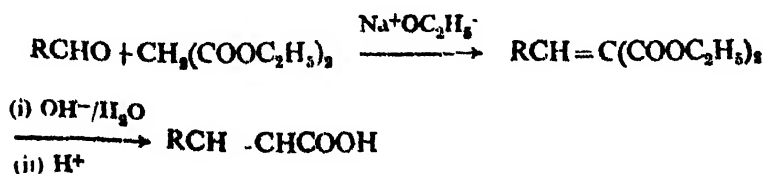
7. *Synthesis of Dicarboxylic Acids*: A dicarboxylic acid is obtained by condensing the sod. derivative of the ester with a halo acid with subsequent hydrolysis of the intermediate.



Adipic acid is obtained by condensing two molecules of malonic ester with ethylene dibromide and then hydrolysing the resultant product.

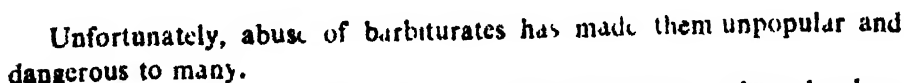


8. *Synthesis of Unsaturated Acids*: The malonic ester is condensed with an aldehyde (aliphatic or aromatic) which is followed by the usual sequence of reactions to give an unsaturated acid.



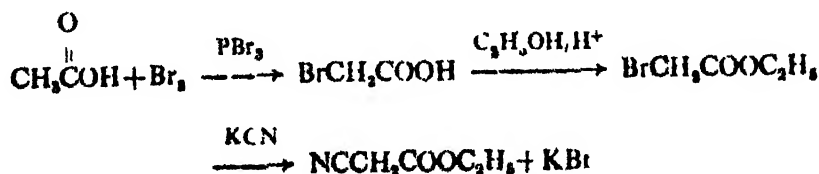
$\text{R} = \text{CH}_3$ (Crotonic acid); $\text{R} = \text{C}_6\text{H}_5$ (Cinnamic acid)

These five drugs have a broad spectrum of physiological activity. *Veronal*, for instance, has a long period, *Amytal* has an intermediate period and *seconal* a short period of action.



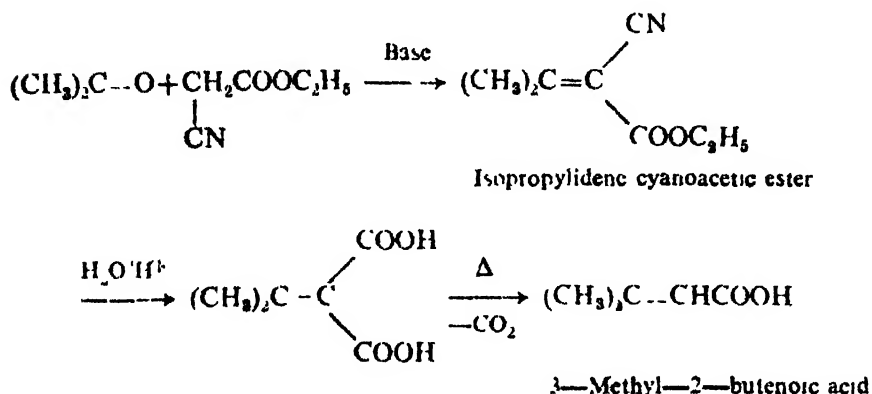
If thiourea is used in place of urea in the condensation, then thio-barbiturates are obtained.

Ethyl cyanoacetate is another important ester which contains an active methylene group. It can be obtained by esterifying bromoacetic acid and subsequent treatment with potassium cyanide.

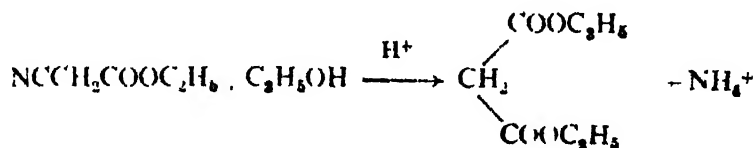


Because of the presence of active methylene group ethyl cyanoacetate also functions as an intermediate in the synthesis of organic compounds. It can be monoalkylated or dialkylated in a manner similar to malonic ester. In a number of cases ethyl cyanoacetate may be employed in place of malonic ester for the preparation of organic compounds.

10. Condensation with Ketones: With ketones, ethyl cyanoacetate forms unsaturated esters which can be further treated to form α , β -unsaturated carboxylic acids.

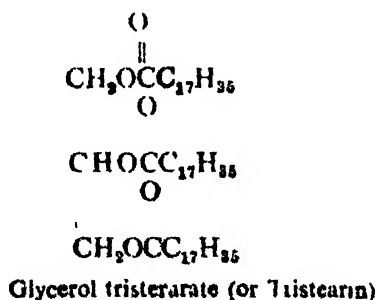


Ethyl cyanoacetate, on treatment with ethanol in the presence of an acid catalyst, forms malonic ester.



19.17 OILS, FATS AND WAXES

The most important of the natural esters are the animal and vegetable oils and fats. These are esters of glycerol (1, 2, 3-propanetriol) with long chain fatty acids. The ester from stearic acid and glycerol has the following structure.



All fats and vegetable oils have one chemical property in common, i.e., when they are heated with sodium hydroxide solution, they produce a mixture containing glycerol and sodium salts of fatty acids.



Glycerol, being a trihydroxy alcohol, forms a triester with fatty acids. These triesters of glycerol are known as *glycerides*.

Oils and fats, besides proteins and carbohydrates, constitute one of the main sources of daily food. Closely related to oils and fats are the waxes and soaps. Together they all belong to the lipid class. The term *lipid* (Greek, Lipos, fat) is used to describe substances that are of natural origin, insoluble in water but soluble in organic solvents. Indeed oils, fats and waxes are examples of lipids.

Oils and fats are differentiated on the basis of their physical states. Fats are solid esters while oils are liquid esters of glycerol. This behavior depends on the aliphatic chain attached to the carboxyl function. If the chain is saturated, then the glycerol ester is generally solid but liquid if it contains unsaturation. Double bonds in the alkyl chain tend to lower the melting point. The most common saturated acids obtained from the hydrolysis of fats are listed below:

Decanoic acid: (C_{10}): $\text{CH}_3(\text{CH}_2)_8\text{COOH}$ (m.p. 32°)

Lauric acid: (C_{12}): $\text{CH}_3(\text{CH}_2)_{10}\text{COOH}$ (m.p. 44°)

Myristic acid: (C_{14}): $\text{CH}_3(\text{CH}_2)_{12}\text{COOH}$ (m.p. 58°)

Palmitic acid: (C_{16}): $\text{CH}_3(\text{CH}_2)_{14}\text{COOH}$ (m.p. 63°)

Stearic acid: (C_{18}): $\text{CH}_3(\text{CH}_2)_{16}\text{COOH}$ (m.p. 70°)

Oleic acid: (C_{18}): $\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$ (m.p. 13°)

Linoleic acid: (C_{18}): $\text{CH}_3\text{CH}_2(\text{CH}=\text{CH}-\text{CH}_2)_2(\text{CH}_2)_6\text{COOH}$ (m.p. 11°)

Some examples of oils are olive oil, linseed oil, peanut oil, soyabean oil, coconut oil, cotton seed oil, etc., and those of fats are beef tallow, butter, etc. These are used for cooking and frying purposes.

Natural fats or oils usually consist of complex mixture of triesters of glycerol though some of them may contain simple and mixed glycerides. Olive oil, for instance, consists of 83% oleic acid, 6% palmitic acid, 4% stearic acid and 7% linoleic acid. Butter oil contains at least fourteen different acids. Butter is a soft fat and owes its physical characteristics both to the presence of lower molecular weight glycerides and to unsaturation. A study of the composition of fats and oils from various sources reveals that palmitic acid is the most abundant of the fatty acid components while oleic acid is the most widely distributed.

19.18 WAXES

Waxes differ from oils and fats in the sense that they are not esters of glycerol but are esters of long chain even numbered fatty acids with long chain even-numbered monohydric alcohols. They contain only one ester linkage against three in oils and fats. Furthermore, waxes cannot be converted into water soluble products by boiling with alkali. Waxes are low melting solids and have a waxy touch. Some examples are *beeswax* (is mainly myricyl palmitate, $C_{15}H_{31}COOC_{30}H_{61}$) it is the material from which bees build honey—comb cells; *carnubawax* (myricyl cerotate, $C_{25}H_{51}COOC_{30}H_{61}$), it occurs as the coating on Brazilian palm leaves; and *spermaceti* (is largely cetyl palmitate, $C_{15}H_{31}COOC_{16}H_{33}$), it separates from the oil of sperm on cooling. Waxes are used in making polishes, cosmetics, ointments and other pharmaceutical products.

19.19 VEGETABLE OILS

These are liquids and contain unsaturated acids. Their principal use is as food.

19.20 ESSENTIAL OILS

These oils are so known because of their essence. Some examples are: lemon oil, clover oil, turpentine oil, etc. They occur in plants and are used in perfume and in pharmaceutical products.

19.21 MINERAL OILS

These are obtained from petroleum and consist of a mixture of saturated and unsaturated hydrocarbons. These oils are insoluble in water and are non-edible. They are mainly used for burning purposes.

19.22 RANCID OILS

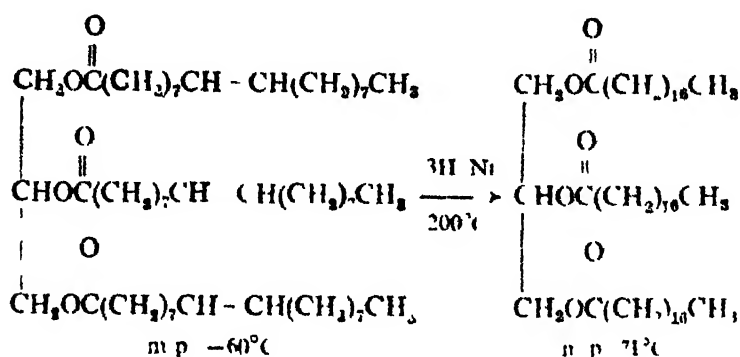
Poly unsaturated glycerides are oxidized by atmospheric oxygen slowly to products such as keto and hydroxy—acids. *Rancid oils* are those in which the oxidation has taken place to some extent and their typical odor is due to the presence of the acid products.

19.23 HYDROGENATION OF OILS

Typical vegetable oils such as cotton seed oil and peanut oil are used extensively for the preparation of fats and soaps. Since the oils are glycerides of unsaturated acids, their melting points can be increased by catalytic hydrogenation of the $C=C$ double bonds. Hydrogenation of oils, also known as hardening, is carried out industrially on a large scale.

The need for the hydrogenation of oils arises because the vegetable oils possess colors and odor and they become viscous and black on keeping. Furthermore food cooked in oils emits odor after it is left for a few days. These drawbacks are not found in the hardened oils. In the process of

hardening, free acid from the edible oils is removed by neutralization with dil sodium hydroxide solution. The resultant oil is washed with water and bleached with animal charcoal followed by deodorization. Hydrogen gas is passed at 200° in the presence of Ni catalyst till a fat of desired consistency is obtained. The resultant fat is tinned and allowed to solidify at a low temperature. Triolein in this manner is converted to tristearin

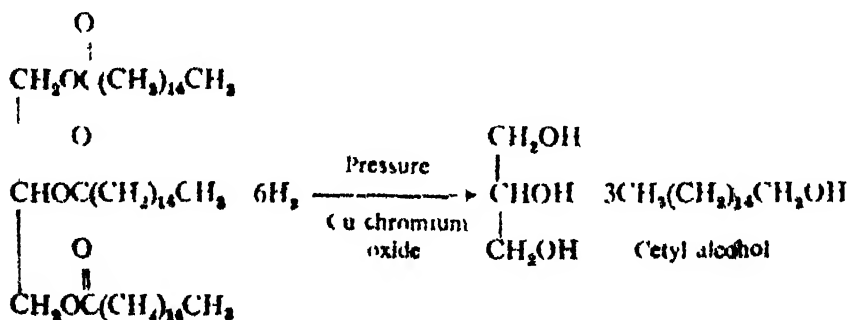


These fats are marketed under different brand names such as *PALMOL*, *RIFF*, *CRISCO*, etc., and are used in the preparation of food products.

The non-edible oils, after hydrogenation are employed for making soaps and cosmetics.

19.24 HYDROGENOLYSIS OF FATS

If the hydrogenation of oil or fats carried out to a state beyond the formation of a saturated fat, *hydrogenolysis* of the ester linkage may take place with the resultant formation of a long chain saturated alcohol and glycerol. This is illustrated below:



Each ester bond requires two moles of hydrogen.

These alcohols are employed in the manufacture of synthetic detergents.

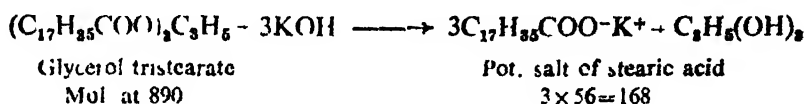
19.25 ANALYSIS OF OILS AND FATS

The length and the nature of the aliphatic side chain attached to the carboxyl function determines the properties of an oil or fat. In order to control the composition and quality of oils and fats for the preparation of various products, the following three analytical methods are employed.

19.25.1 Saponification Number

Fats and oils may be saponified quantitatively. The *saponification number* is defined as the number of milligrams of potassium hydroxide required to hydrolyze one gram of a fat or oil. This value gives an average molecular weight of a fat or an indication of the length of the carbon chain of the fatty acid component. The higher the saponification number of a fat, the greater the percentage of short-chain and low molecular weight glycerides it contains. Thus coconut oil and butter with short chain fatty acids, have saponification numbers of 250—260 and 216—235 respectively. The saponification number of other oils such as olive oil, cottonseed oil, soyab an oil, linseed oil, etc., ranges from 185 to 200.

The saponification number for any pure glyceride is calculated by the following equation.



$$\text{Saponification number} = \frac{168}{890} \times 1000 = 189$$

19.25.2 Iodine Number

It represents the number of grams of iodine which will combine with one hundred grams of the oil or fat. It is a measure of the degree of unsaturation. The more the number of double bonds in the fat the greater will be the iodine number. To determine this, a known weight of the sample is dissolved in CHCl_3 and then Wij's solution (iodine chloride dissolved in acetic acid) is added. Iodine adds to $\text{C}=\text{C}$ bond to form a diiodo derivative. After keeping for some time, KI solution is added and the unreacted iodine is titrated against standard potassium thiosulfate solution using starch indicator. The iodine number is calculated as follows:

$$\text{Iodine number} = \frac{(V_1 - V_2) \times N \times 127 \times 100}{W \times 1000}$$

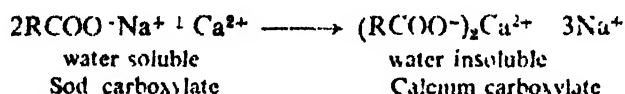
where V_1 = volume of thiosulfate solution for blank; V_2 = volume of thiosulfate solution for the sample; N = normality of thiosulfate solution and W = weight of the sample.

The mixture is then saturated with NaCl. The salt, due to common-ion effect reduces the solubility of soap which precipitates out. The impure soap contaminated with alkali, glycerol and salt is separated from the aqueous solution. The crude soap is purified by boiling with water and reprecipitating with NaCl. This process is repeated several times. Soap may then be converted into medical soap by the addition of disinfectants and to toilet soap by the addition of perfume and color. Potassium salts are employed in the manufacture of liquid soap and shaving creams. Soap is marketed in the form of cakes and bars, chips and flakes; in grain and in solution.

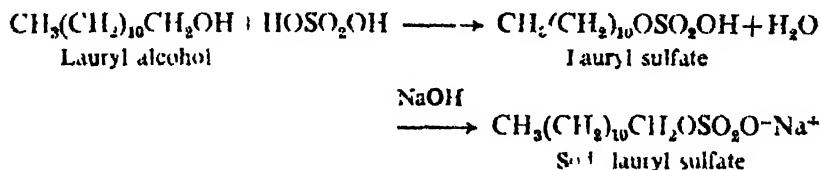
In order to show effective soap action, the fatty acid must contain at least 12 carbon atoms. On the other hand, molecules containing more than 22 carbon atoms are not useful because of their insolubility in water.

19.27 SYNTHETIC DETERGENTS

Sodium soaps are soluble in water but form insoluble salts when used in hard water and precipitate out as calcium, magnesium or ferric salts because hard water contains these ions.



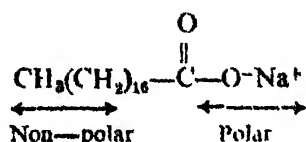
This causes difficulty in cleaning and also much soap is wasted. Since 1948, there has been a great interest in the manufacture of synthetic soap known as *detergents*. Detergents also possess the same structural features as soaps namely an ionic group and a long chain non-polar organic group. Among the most important detergents are the sodium salts of sulfonic acids. Long-chain alcohols are converted into derivatives of sulfonic acid which are then neutralized with sodium hydroxide.



These sulfonates do not form insoluble salts with Ca, Mg, or Fe ions. This is a great advantage with detergents and they can be used in hard water as well. Detergents are cheap to make. They are, however, non-biodegradable and cause foaming in rivers and canals.

19.28 CLEANING ACTION OF SOAP

The mechanism of the cleaning action of soap is related to its chemical structure. A soap molecule consists of two parts, mainly a polar, salt-like carboxylate function and a non-polar, long alkyl chain as shown below:



The polar part is hydrophilic (water soluble) whereas the non-polar portion is hydrophobic (water insoluble or oil soluble). A typical soap molecule, sod. stearate has both an oil soluble and water soluble portion. A sodium salt of a smaller carboxylic acid is soluble in water but if this hydrocarbon residue is long then the hydrocarbon portion causes the soap to become insoluble.

There are several theories to explain the cleaning action of soap. Soap greatly reduces the surface tension of water. Thus soap is able to enter into tiny cracks and crevices. Soap also has the ability to emulsify fats and oils and thus greatly assists in their removal.

According to another theory the charged carboxyl group at the end of the soap chain enables it to dissolve in water. When soap dissolves, it does so in the form of spherical clusters called micelles (Fig. 19.1). The non-polar hydrocarbon chain mixes well with the greasy substances.

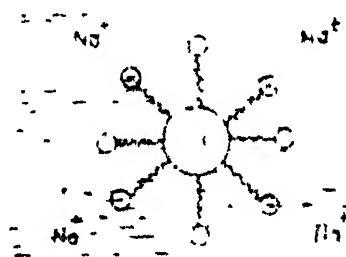


Fig. 19.1 A soap micelle

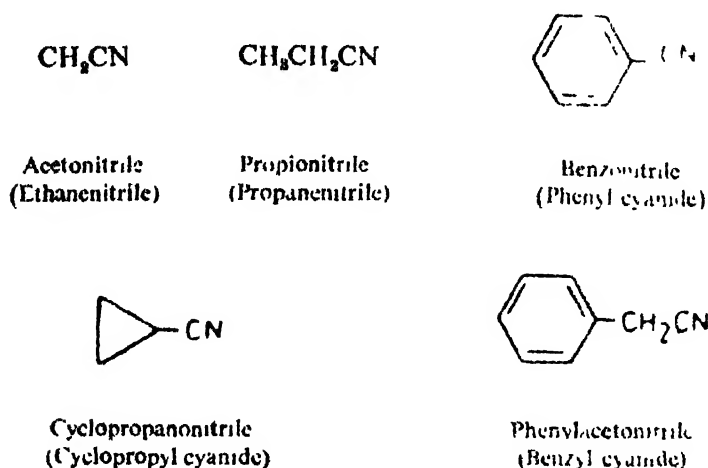
When soap water comes in contact with grease, the non-polar chain dissolves grease which is also non-polar. This leaves the grease surrounded by an outer layer of groups which are attracted towards water. The forces between water and grease are much increased so that the latter is lifted off the surface of water in the form of small globules and can be washed away. The layer of negatively charged groups causes the globules to repel one another so that they do not coagulate and redeposit on the surface of the cloth.

19.29 NITRILES AND *iso* NITRILES

Nitriles may also be considered as functional derivatives of carboxylic acids because they also yield acids on hydrolysis. They are also known as cyanides or cyano compounds.

Nitriles are named according to the carboxylic acid they yield on hydro-

lysis. The name is derived by replacing the suffix *-oic* of the acid by *-onitrile*. In the IUPAC system they are named as alkane nitriles.



The *iso* nitriles are named either as the alkyl isocyanides or using the prefix *iso* before the name of the carbonitrile. In the IUPC system they are named as alkyl carbylamines.

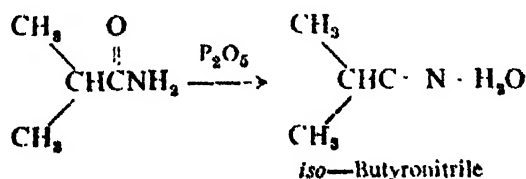


Alkyl cyanides are pleasant smelling while the isocyanides have disagreeable odor. They are soluble in organic solvents. Alkyl cyanides are less poisonous than hydrogen cyanide.

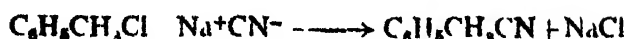
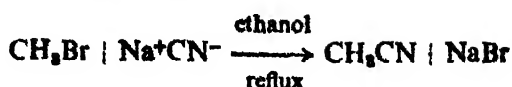
Preparation

Several methods are available for the preparation of both nitriles and isonitriles.

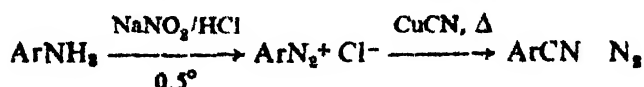
1. *Dehydration of Amides*: An efficient dehydrating agent such as P_2O_5 dehydrates an amide to a nitrile. This is a useful method for preparing nitriles.



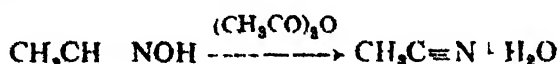
2. An $\text{S}_{\text{N}}2$ displacement of a halide ion from alkyl halide by the cyanide ion using ethanol as the medium affords a nitrile and constitutes a most convenient method for their preparation.



3. Aryl cyanides are also obtained by the Sandmeyer reaction



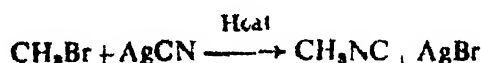
4. *Dehydration of Aldoximes* Aldoximes in the presence of acetic anhydride or PCl_5 also yield cyanides.



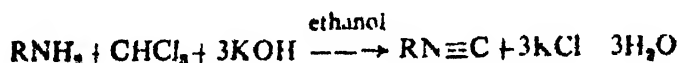
5. In the commercial production of acetonitrile, a mixture of acetic acid vapor and ammonia is passed over a dehydrating agent at high temperature



6. An alkyl isocyanide may be obtained by heating an alkyl halide with AgCN .

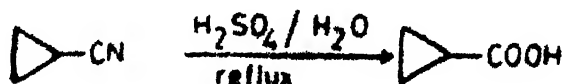
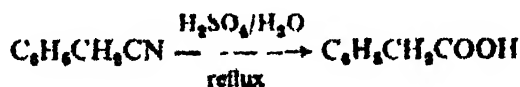
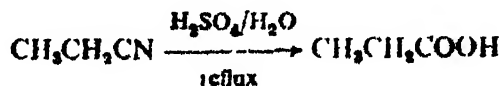


It may also be obtained by heating a primary amine with chloroform in the presence of alcoholic KOH solution.

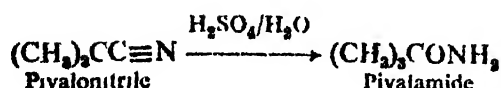


Reactions

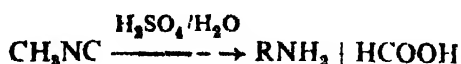
1. *Hydrolysis* A cyanide requires either an acid or base for hydrolysis. The product is a carboxylic acid and in the mechanism an amide is postulated as an intermediate.



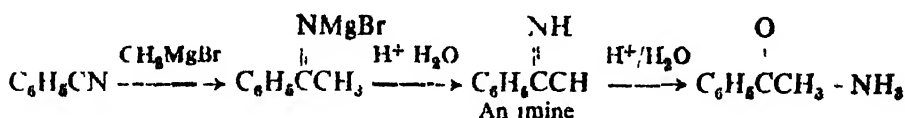
If the nitrile is sterically hindered, the amide, rather than the acid is usually obtained.



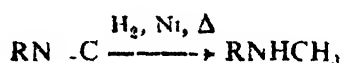
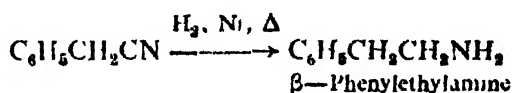
iso Cyanides yield amines on acid hydrolysis.



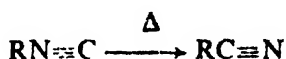
2. A cyanide adds on a molecule of the Grignard reagent and the imine intermediate is further hydrolyzed to a ketone.



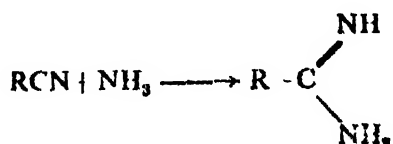
3. *Reaction*: Cyanides are reduced to primary while *iso* cyanides are reduced to secondary amines



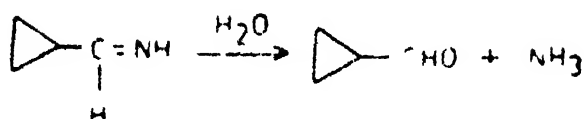
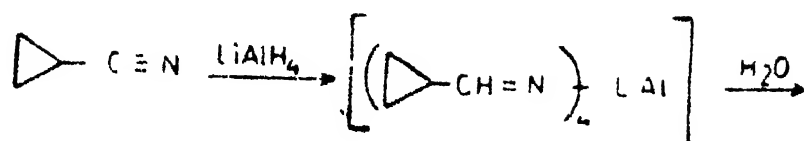
4. Isocyanides rearrange on heating for a long time to cyanides.



5. Alkyl cyanides combine with dry ammonia to form amidines.



6. Alkyl cyanides can be converted into aldehydes and they thus provide a useful method for their preparation. Lithium aluminum hydride in ether reduces a cyanide under controlled conditions to an imine which on hydrolysis forms an aldehyde.



An imine

Cyclopropane carboxyaldehyde

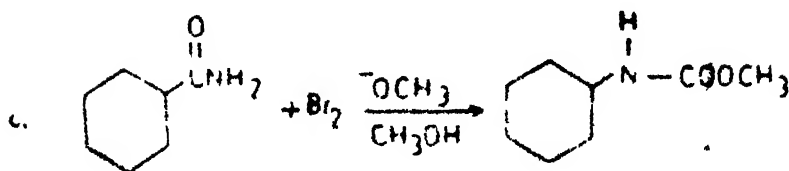
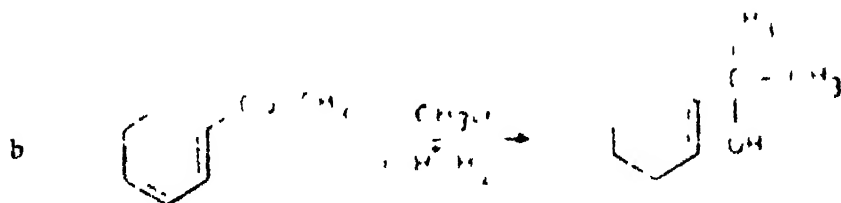
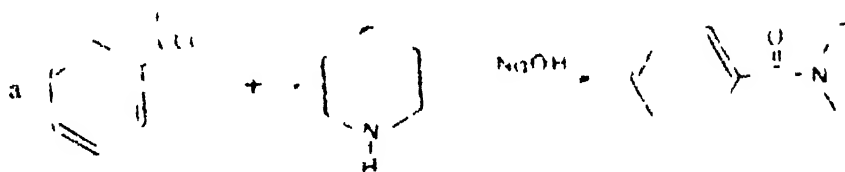
QUESTIONS

19.1 Write short notes on the following:

1. Esterification of an acid, waxes, synthetic detergents, acidity of amides, hydrogenation of oils, saponification number

19.2 Describe the preparation, reactions and uses of urea

19.3 Write a mechanism for each of the following reactions



19.4 Show by chemical equations how to make soap from fat.

19.5 Write structural formula for the following compounds:

- a. N-Ethylbutanamide
- b. *p*-Bromobenzoyl chloride
- c. Propionic anhydride
- d. *n*-Hexyl hexanoate
- e. 2, 3-Dimethyl succinimide
- f. *m*-Cyanotoluene
- g. Cyclohexane carboxamide
- h. Ethyl butyrate
- i. *iso* Propyl butyrate
- j. α -Bromopropionitrile
- k. 2-Naphthyl hexanoate
- l. 2-*iso* Propyl heptanenitrile
- m. Diazomethane
- n. *iso*-Butyric acetic anhydride
- o. Ethyl-2-(4-methyl cyclohexyl) propionate
- p. Cyclopropanecarboxylic acid chloride

19.6 Show how each of the following conversion could be accomplished:

- a. Acetyl chloride to acetic anhydride
- b. Benzoyl chloride to ethyl benzoate
- c. Acetic anhydride to acetone
- d. Ethyl acetate to 3-methyl-3-pentanol
- e. Trimethylacetic acid to *t*-butyl isocyanate
- f. Ethyl propionate to propionitrile
- g. Propionitrile to ethylamine
- h. Ethyl acetoacetate to antipyrine
- i. Malonic ester to leucine

19.7 Discuss the preparation, important reactions of nitriles and *iso*-nitriles.

19.8 Write the structural formulas for all the esters of the formula $C_5H_{10}O_2$. Write their IUPAC names also.

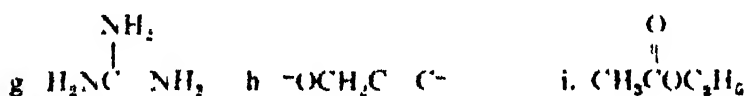
19.9 Write equations to show the reactions of butanoyl chloride with the following reagents

- a. Benzene $AlCl_3$
- b. Water
- c. *iso*-propyl alcohol
- d. Aniline
- e. Dimethylaniline
- f. Sodium acetate and heat
- g. Trimethylamine

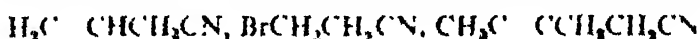
19.10 An ester $C_9H_{18}O_2$ was hydrolyzed with water and an acid, A, and an alcohol, B were obtained. Oxidation of B, with chromic acid

produced A. What is the structure of the original ester? Write equations for all the reactions.

- 19.11 A neutral liquid of formula $C_7H_{14}O_2$ is hydrolyzed to an acid A, and an alcohol, B. Acid A, has a neutralization equivalent of 84. Alcohol B, is not easily oxidized with an acid solution of sodium dichromate. What is the formula and name of the original compound?
- 19.12 An ester of molecular formula $C_8H_{16}O_2$ on hydrolysis affords an acid A and an alcohol B. Oxidation of alcohol B with sodium dichromate gives rise to an acid C. Sodium salts of acids A and C on fusion with solid sodium hydroxide yield propane in each case. What is the structural formula of the original ester?
- 19.13 In each of the following cases give the monoprotinated product and justify your answer. Note that in some cases there are two sites for monoproteination.



- 19.14. Hydrolysis of a nitrile requires the presence of an acid or base. Which of these two would you expect to be employed in the following cases because of the sensitivity of other functional groups?



- 19.15 Write the reactions involved in the preparation of the following compounds using the reagents indicated in parentheses:

a. Methyl benzoate from benzene (CH_2Cl , $AlCl_3$, $Br_2/h\nu$, Mg ether, CO_2/H^+ , CH_3OH/H^+).

b. Propionic anhydride from propionaldehyde



c. Benzanilide from benzoic acid ($SOCl_2$, $Cd(C_6H_5)_2$, H_2NOH , H^+).

- 19.16 Describe the preparation of diethyl malonate. How can it be used to synthesize,

(i) *iso* Butyric acid (ii) Barbituric acid (iii) Crotonic acid (iv) Acetoacetic acid.

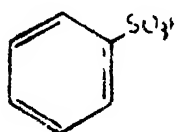
- 19.17 What is a reactive methylene group? Illustrate your answer by

giving the synthetic uses of a compound containing a reactive methylene group.

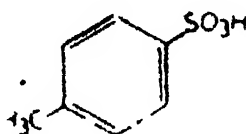
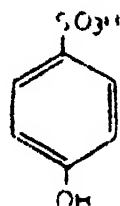
- 19.18 What are vegetable oils and how do they differ from mineral oils? Starting with a suitable mixture of oils, give a detailed account for the manufacture of soap? Write a short note on synthetic detergents.
- 19.19 a. Briefly State how ethyl acetoacetate is prepared.
b. How will you prove the existence of the keto and enol forms the ester?
c. Making use of the ester how can you prepare:
(i) Succinic acid (ii) *iso* Butyric acid (iii) Methyl ethyl ketone.
- 19.20 (a) What is "active methylene" group? Explain.
(b) How will you prepare:
(i) adipic acid from malonic ester (ii) methyl ethyl ketone from acetoacetic ester (iii) crotonic acid from acetoacetic ester?
- 19.21 Describe the keto-enol tautomerism with reference to ethylacetoacetate. Mention two synthetic uses of this ester.
- 19.22 a. Discuss the chemistry and industrial uses of oils and fats.
b. Explain the significance of saponification value.
- 19.23 What are fats and oils? What is the importance of hydrogenation and hydrolysis of fats and oils? Explain with example.
- 19.24 a. What is the natural source of urea? How is it synthesized? What are its important uses?
b. Explain what happens when urea is:
(i) heated alone (ii) treated with alkaline hypobromite solution (iii) treated with malonic ester (iv) treated with ice-cold nitrous acid (v) treated with hydrazine.
- 19.25 Calculate the saponification number of tristearin of 90% purity.
- 19.26 Give an example of a detergent. Discuss the cleaning action of soap.

Sulfonic Acids, Their Derivatives and Drugs

Sulfonic acids are another important class of organic acids. Both aliphatic and aromatic sulfonic acids are known but we will limit the discussion to the aromatic sulfonic acids only. These acids possess the general molecular formula $ArSO_3H$ where $-SO_3H$ is called a *sulfonic acid group*. These are strong acids and ionize completely in solution. The names of the acids are simply derived by adding the *suffix* sulfonic acid to the name of the compound to which $-SO_3H$ function is linked. Following are some representative examples:



Benzenesulfonic acid

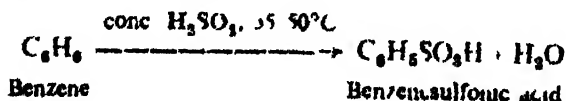
*p*-Toluenesulfonic acid*p*-Hydroxybenzene sulfonic acid

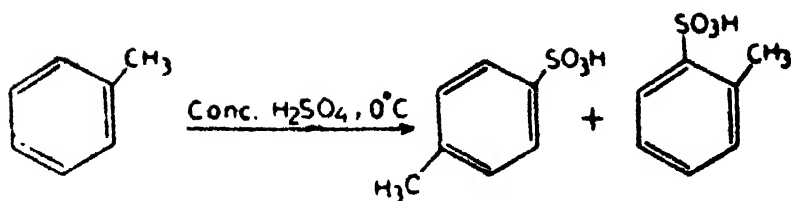
20.1 PHYSICAL PROPERTIES OF SULFONIC ACIDS

Sulfonic acids are highly polar and very soluble in water, but insoluble in most organic solvents. The sulfonic acid group is often introduced to prepare tailor-made compounds to bring about water solubility. Benzenesulfonic acid is comparable in acidity to sulfuric acid.

20.2 PREPARATION OF SULFONIC ACIDS

1. Sulfonic acids are prepared by sulfonation of the corresponding hydrocarbons. Different reagents employed for sulfonation are sulfuric acid, (H_2SO_4) chlorosulfonic acid $(ClSO_3H)$ or fuming sulfuric acid $(H_2SO_4 \cdot SO_3)$, also known as *oleum*.

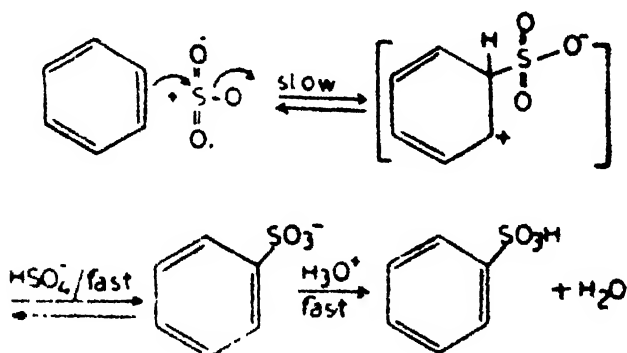
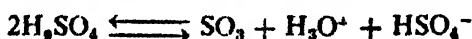


**Mechanism**

The mechanism of the reaction resembles that of halogenation and nitration.

The attacking electrophile in sulfonation is SO_3 , $\begin{array}{c} \text{O} \\ \parallel \\ (\text{S}=\text{O}) \\ \parallel \\ \text{O} \end{array}$. It is a power-

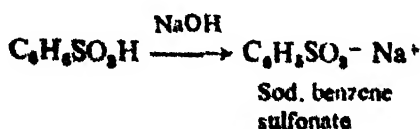
ful electrophile and reacts directly with the benzene ring. The concentration of SO_3 in sulfuric acid may be regarded as due to the self-reaction of sulfuric acid. All the steps in the mechanism are reversible. It is a normal electro-

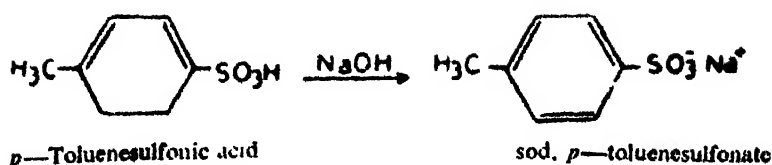


philic aromatic substitution reaction. The difference, however, is that the intermediate does not have a net formal charge, rather it is neutral. The product of the reaction is benzenesulfonic acid which is purified and often used in the form of its sodium salt.

20.3 REACTIONS OF SULFONIC ACIDS

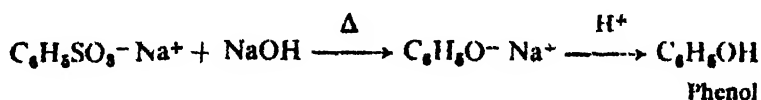
1. **Salt Formation:** Unlike aromatic carboxylic acids, aromatic sulfonic acids are completely ionized in water and form salts with bases.



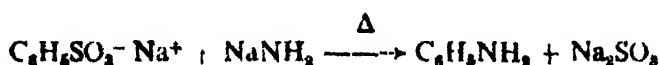


The acid evolves CO_2 with sod. bicarbonate.

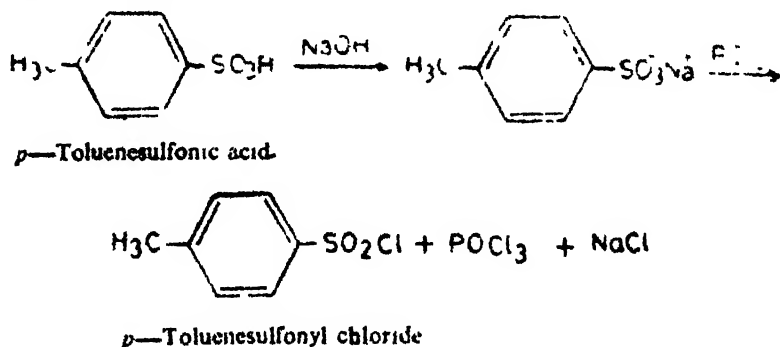
2 *Fusion with Alkalies*: The sulfonic acid group can be replaced by a nucleophile under drastic conditions. With sodium hydroxide it requires fusion ($250\text{--}300^\circ$) and gives rise to phenol.



The sodium salt of the acid on fusion with sodamide yields aniline.

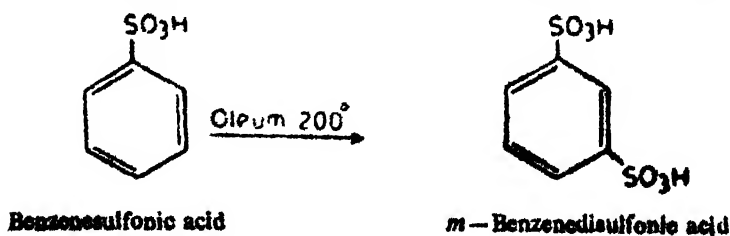


3. *Formation of Acid Chloride*: A sulfonic acid can be converted to an acid chloride by reaction with PCl_5 . For this purpose it is convenient to work with the sodium salt of the acid.

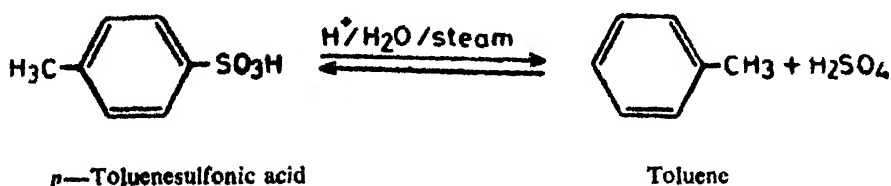


The sulfonyl chloride and not the acid reacts directly with alcohols or phenols.

4. *Ring Substitution*: The $-\text{SO}_3\text{H}$ group is an electron-withdrawing and thus *m*-directing. Nitration or sulfonation yields *meta* derivatives of the acid.

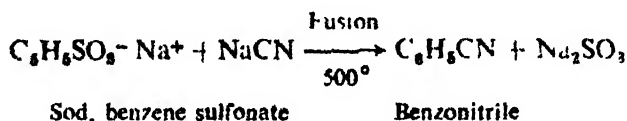


5. **Desulfonation:** This is the reverse of sulfonation and takes place when a sulfonic acid is heated at 100–175° with aqueous sulfuric acid. The



reaction is reversible and to push it to the right a dilute acid is used and superheated steam is passed through the reaction mixture. Furthermore, the volatile hydrocarbon is continuously removed.

6. The $-\text{SO}_3\text{H}$ group can be replaced by $-\text{CN}$ by fusing the sodium salt of the acid with NaCN



The yields in this reaction are often poor.

20.4 USES OF SULFONIC ACIDS

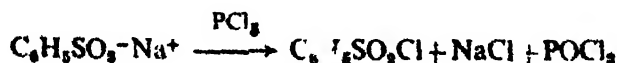
Sulfonic acids are commonly employed for the preparation of naphthalene derivatives, where preparation of nitriles through an intermediate halide or amine are not feasible. They are used in organic synthesis, for the manufacture of phenol, dyes and in synthetic detergents.

20.5 BENZENESULFONYL CHLORIDE

Benzenesulfonyl chloride is one of the most important derivatives of benzene sulfonic acid.

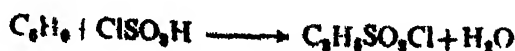
Preparation

1 It is prepared by treating the sodium salt of the acid with phosphorus pentachloride.



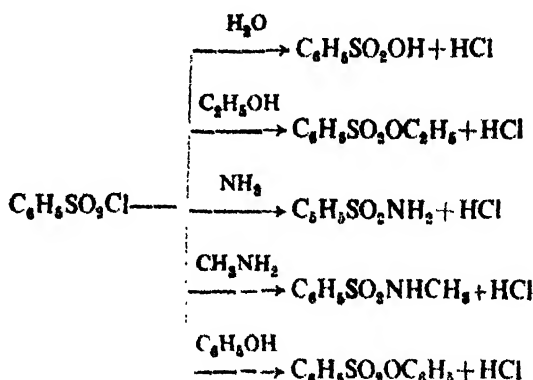
Pure benzenesulfonyl chloride is obtained by distillation (b.p. 251.5°).

2. Benzenesulfonyl chloride may also be obtained by direct chlorosulfonation of benzene.



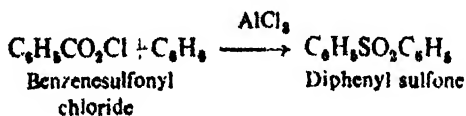
Reactions

1. Benzenesulfonyl chloride reacts with water, ammonia, alcohol or phenol to yield the corresponding acid derivatives.

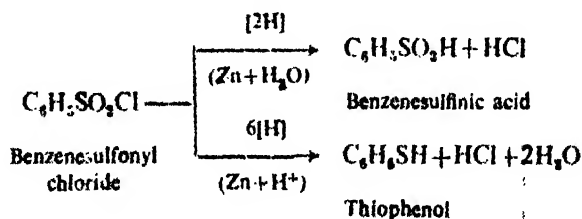


Sulfonic esters are prepared by the reaction between sulfonyl chloride and an alcohol, and not directly from sulfonic acids

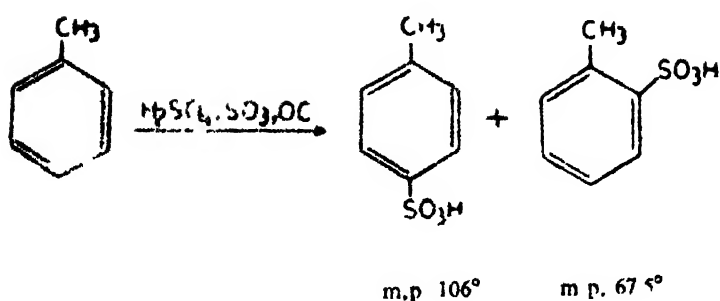
2. **Friedel—Crafts Reaction:** Benzenesulfonyl chloride reacts with benzene under the Friedel—Crafts conditions to form sulfones.



3. Sulfonyl chlorides, in contrast to sulfonic acids can be readily reduced to sulfinic acids or thiophenols.

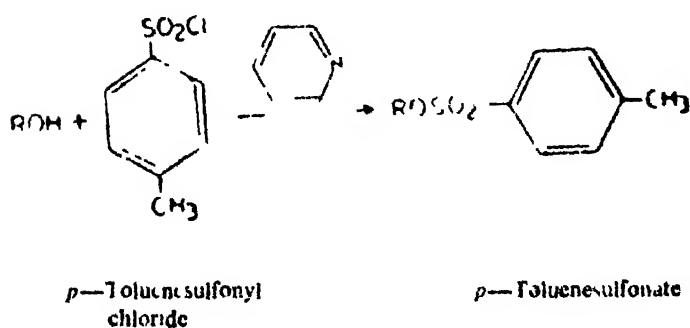
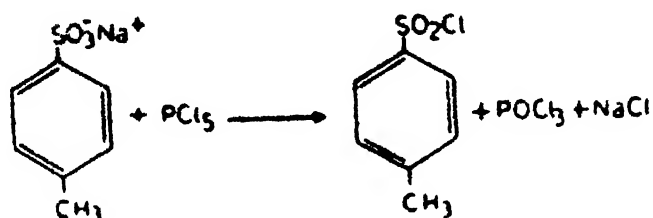
**20.6 *p*-TOLUENESULFONIC ACID****Preparation**

1. The isomeric *o*- and *p*-toluenesulfonic acids may be obtained by sulfonation of toluene in the presence of sulfuric acid at low temperature.

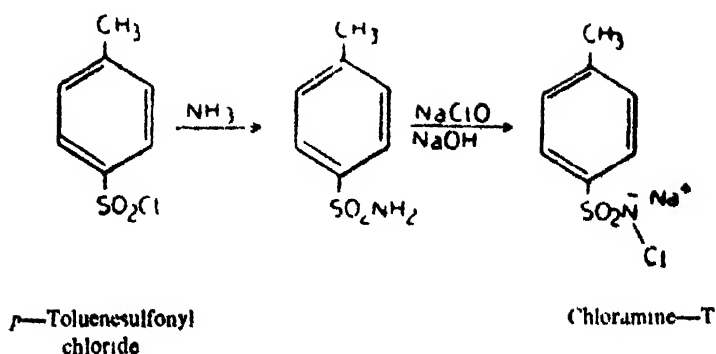


Reactions

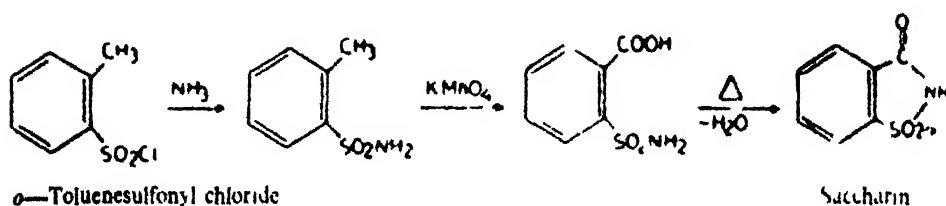
1 The sodium salt of the acid with PCl_5 , forms *p*-toluenesulfonyl chloride. *p*-Toluenesulfonyl chloride is also known as *tosyl chloride* and is used in the preparation of tosyl esters from alcohols



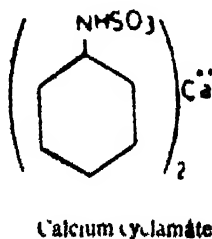
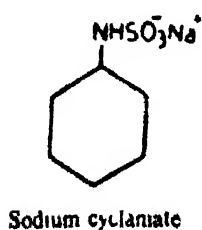
2 It is used in the preparation of chloramine-T (sod. *p*-toluenesulphonchlorpamide). For its preparation, toluene is converted to toluene-4-sulfonyl chloride which is heated with ammonia to form the amide. Subsequent reaction with sod. hypochlorite gives chloramine-T



3. The *o*-isomer is used in the preparation of saccharin [3-Oxo-2,3-dihydrobenz [d] isothiazole-1,1-dioxide]

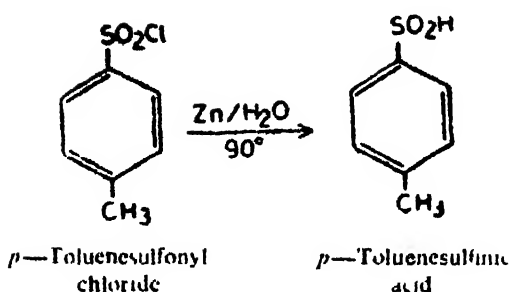


Saccharin is used as artificial sweetener in soft drinks. It is 600 times sweeter than sugar. It has no food value and is excreted unchanged in urine. Saccharin is unpalatable to many people because it leaves a bitter after-taste. It was replaced by cyclamates, which though only 15 times sweeter than sugar, leaves no after-taste. The structures of these compounds are:



Even this sweetener was found to cause bladder cancer in rats, therefore, the research for new artificial sweeteners is continuing.

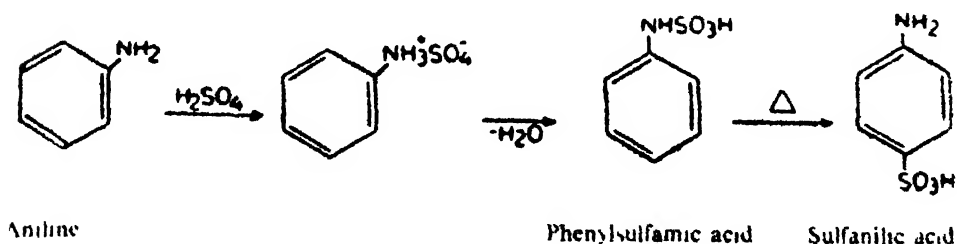
4. *p*-Toluenesulfonyl chloride can be reduced with zinc and water to form sulfinic acid.



20.7 SULFANILIC ACID

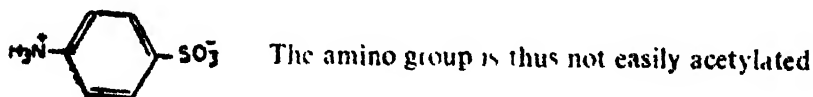
Preparation

Sulfanilic acid or *p*-aminobenzenesulfonic acid is prepared by heating aniline with sulfuric acid at 180–190° for about 5 hours. Aniline hydrogen sulfate is first formed which loses a molecule of water to form phenylsulfamic acid which rearranges to sulfanilic acid.

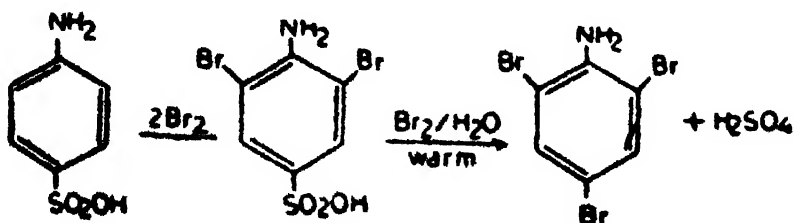


Reactions

1 Sulfanilic acid is grey in color due to atmospheric oxidation. It exists in the form of an internally ionized salt, i.e., a "zwitterion" (a dipolar ion)



2. **Bromination** · Bromination of sulfanilic acid first gives 3,5-dibromo-4-aminobenzenesulfonic acid which on warming with excess bromine yields 2,4,6-tribromoaniline

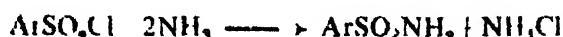
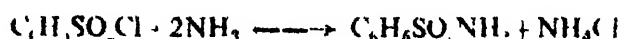


Uses

Sulfanilic acid is a valuable intermediate for the preparation of several dyes such as methyl orange.

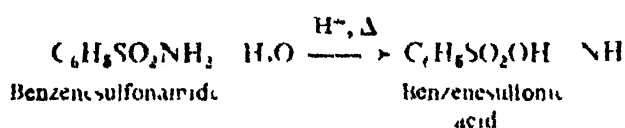
20.8 SULFONAMIDES**Preparation**

1 Treatment of ammonia with sulfonyl chlorides yields sulfonamides

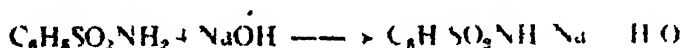
**Reactions**

Sulfonamides are crystalline solids with sharp melting points

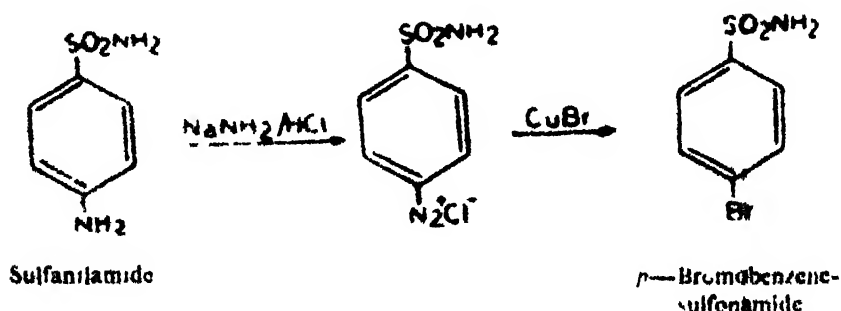
1 On heating benzenesulfonamide with aqueous acids, sulfonic acid and ammonia are formed. A sulfonamide, however, undergoes hydrolysis much more slowly than an amide of a carboxylic acid



2. Sulfonamides show appreciable acidity and dissolve in strong alkalis to form water soluble salts



3. Sulfanilamides react very slowly with HNO_2 and use is made of this property to diazotize the ring amino group without attacking the sulfonamide group

**20.9 DRUGS**

A drug may be defined as any chemical agent that affects the protoplasm,

i.e. the body cells. The proper functioning of the body depends on different chemical reactions and a breakdown in these reactions results in an abnormal condition which we call *disease*. To combat diseases we need drugs. In the past almost all medicines used by doctors came from plants, being extracted from leaves, roots or seeds. The extract was made up in the same way as we make tea or coffee, a cup of tea being an infusion of the leaves of the tea plant. The development of synthetic drugs was most marked in Germany and was closely related to the development of techniques in organic and analytical chemistry. Certain drugs tend to have more than one physiological effects some of which can be detrimental. A substantial part of research nowadays is directed to minimize the side effects, besides achieving its goal of combating the disease.

20.9.1 Drug Action

There are several theories about the action of drugs. However, before a drug can exert its characteristic effect, it must be conveyed to its site of action, therefore, such physical properties as solubility and volatility are of the greatest importance. Drugs taken by mouth should be capable of being absorbed into the blood stream. An additional important factor is that the drug should not be excreted or converted into an inactive form too rapidly.

There are two broad views about the mechanism of drug action. The first is called the *non-specific drug action* which depends on some physical property. The molecular size, shape or nature of the drug has little action on the drug action. The most familiar drugs in this class are the anaesthetics such as ether and chloroform. The property which is responsible for their sleep producing effect is due to their solubility in fats.

The second view is known as the *specific drug action*. According to this, the effect of a drug is markedly dependent on the chemical constitution and the molecular geometry of the molecule. This is based on the concept of *drug receptor interaction*. A receptor is a molecule with which a drug interacts to produce its typical biological and physiological response. In most cases a receptor is often an enzyme. For a drug to be effective it must fit the receptor to form a complex. It is thus anticipated that even a small change in the structure of the molecule would destroy the fit and alter the resultant action of the drug. For instance, it is established that the *levo* form of morphine is active as a pain killer whereas the *dextro* form does not fit the receptor. This mechanism may be envisaged analogous to the action of an enzyme for the progress of a biochemical reaction where a specific enzyme is needed for a particular reaction.

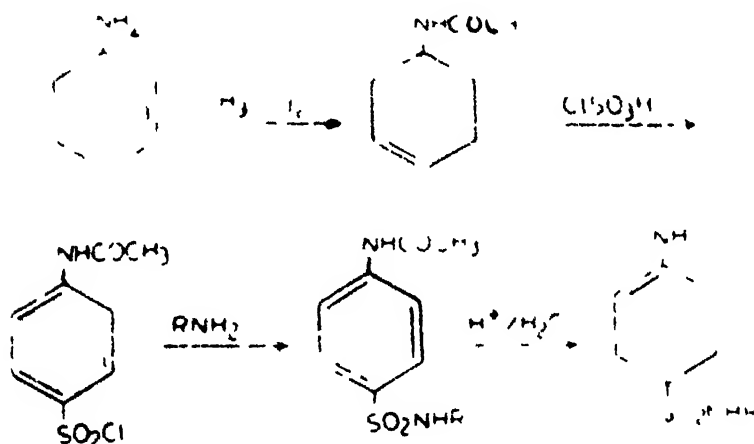
20.10 SPECIFIC DRUGS

The science of drugs, known as *pharmacology*, is very complex and embraces a knowledge of both chemistry and biochemistry. Drugs can save lives if

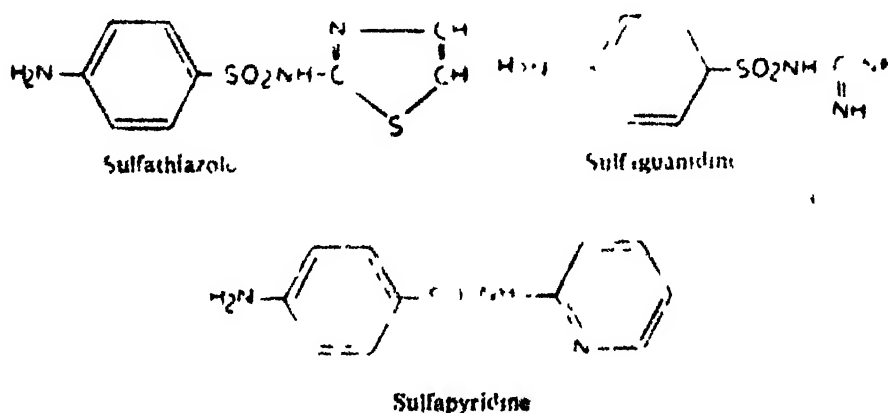
properly used but can become poisons if abused. Several classes of drugs of common use will be discussed here.

20.10.1 Bactericidal

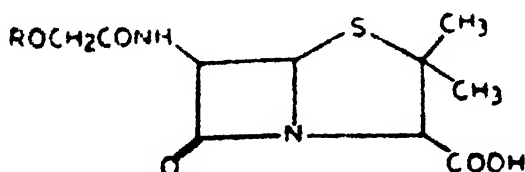
This term denotes anything that destroys bacteria. Though the body tries to defend itself against a disease, defence can be aided with the help of chemical agents. The synthetic chemical agents are known as *chemotherapeutic agents*. Some of the compounds used earlier were the *sulfa drugs* or *sulfonamides*. The first preparation of a sulfonamide (*p*-aminobenzene sulfonamide) was made during the investigations on azo dyes by *Gelmo* in the beginning of the nineteenth century. The synthesis of a sulfonamide is illustrated as follows



The use of a compound as a drug dictates the nature of the amine (RNH_2) and the heterocyclic compounds have proved the most useful. Examples of a few sulfa drugs are given below



Antibiotics: The antibiotics are the naturally occurring chemotherapeutic agents. They have largely replaced the sulfa drugs though the latter still find uses. These substances are more toxic to the microorganisms than to the host. Diseases known to be caused by bacterial infection are treated by antibiotics. The notable success came with *penicillin*. It is a product of the metabolism of the mould *penicillium notatum*. Its discovery was made by Sir Alexander Fleming in 1929 who received the Nobel Prize in medicine in 1945. Like the sulfonamides, penicillin affects only certain types of bacteria. The general formula for penicillins is the following:

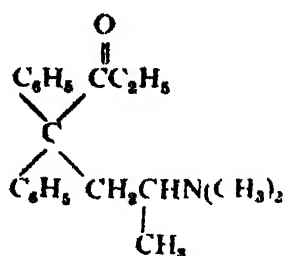


If $R = -CH_2C_6H_5$, then it is called penicillin G.

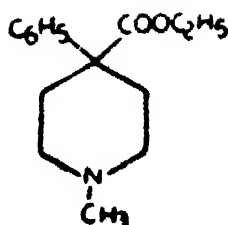
Nowadays several thousands of antibiotics are known but only sixty of them are in clinical use and are employed to treat rheumatic fever, scarlet fever, syphilis, meningitis, tetanus, etc. Tetracycline, streptomycin, and erythromycin have the same antibacterial spectrum. These are the most commonly and casually prescribed drugs. They can be life-saving drugs but their unnecessary use may cause problems like allergy, gastro-intestinal upsets and sensitization of the skin.

20.10.2 Analgesics

These are pain killers. Pain is a syndrome of sensations with which all human beings become inevitable familiar and drugs that can relieve pain are the most sought-after medicines. Such drugs are consumed by people in large numbers even without prescription. Salicylic acid has been used in earlier days for relieving headaches and for lowering the body temperature. But salicylic acid is unpalatable, therefore, its derivatives, like aspirin are used. Morphine, isolated from poppy seeds has a high potency for killing pain. It is the chief alkaloid present in *opium*. Heroin which is a diacetyl derivative of morphine can be prepared in the chemical laboratory and is four times more effective than morphine. These drugs, no doubt, relieve pain and anxiety but at the same time they also cause addiction. Two synthetic drugs, namely methadone and pethidine are free from these drawbacks. Both of these are of German origin. Methadone is also recommended for morphine addicts.



Methadone



Pethidine

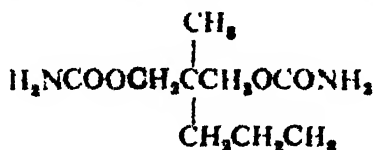
20.10.3 Barbiturates and Amphetamines

Both these types of drugs alter the mental state. Barbiturates are drugs used for inducing sleep (hypnotic agents). These are not obtained from plants but are prepared in the laboratory by condensing urea with malonic acid. The sleep induced by barbiturates is very much like the natural sleep and thus there is a little evidence that barbiturates do any harm. Many of them are sold under trade names.

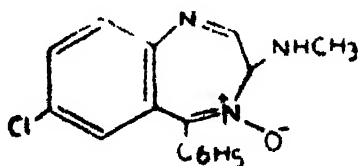
Amphetamines stimulate the central nervous system and are commonly called the 'pep' pills. These are also synthetic drugs and belong to a class of drugs known as *psychic energizers*. These are marketed under the name methedrine, benzedrine and dexedrine.

20.10.4 Tranquillizers

These are drugs which sedate without inducing sleep. Many of them are mild and used to relieve anxiety, excitement and restlessness. These are useful drugs if prescribed properly but giving these drugs for minor worries and stress is definitely a misuse. Meprobamate (trade name equanil) is used to relieve tension without causing drowsiness. Chlordiazepoxide (trade name *librium*) has been used extensively in the treatment of neurosis, behavior disturbances and alcoholism. These drugs are addictive.



Meprobamate



Chlordiazepoxide

Calmose and *Larpose* are the other tranquillizers in common use.

20.11 DRUG ABUSE

Because of the availability of drugs, most diseases can now be easily controlled. Drugs have become a part of our daily life. Several types of drugs have certainly helped in eliminating various diseases and controlling many others. The main hazard of drugs is their abuse. Certain drugs are considered to lead to certain medical and social problems and are known as 'pep'

drugs. Such drugs are consumed for non-medical use and for pleasure-seeking experiences which lead to drug addiction. These drugs include morphine, heroin, cocaine, amphetamines, barbiturates, LSD, alcohol, etc.

Morphine and heroin were originally used for therapeutic purposes but when taken repeatedly they cause addiction. They are also known as *narcotics*. Morphine produces a feeling of well-being, an euphoria especially when it is given by injection into the vein. Addiction to morphine, like addiction to alcohol is a sign of weakness of personality, lack of will power and self respect. Addiction arises because morphine not only diminishes pain but also diminishes worry and anxiety created by the problems of life. Under the influence of morphine, the feeling of frustration disappears and the subject forgets the goal he has set himself and the disappointment in failing to achieve it. Heroin is much more powerful than morphine. Codeine (methyl morphine) is useful as cough depressant. Cocaine was used extensively in surgery. It is not a narcotic, instead it stimulates the brain and it is for this effect that it is taken by addicts.

Amphetamines, barbiturates and tranquillizers as discussed earlier serve various useful purposes in medicine. These are what is known as 'over-the-counter' drugs and people take them of their own. These drugs are habit forming and the patient often wants a tranquillizer to face even the simple problem of life. There is a tremendous misuse of these drugs. Often *marijuana* and other derivatives of cannabis (Indian hemp) such as *hushish* (resinous extract) are discussed as hallucinogens. *Hallucinogens* are often known as *psychedelics* or *psychomimetics* drugs, which causes transient changes in perception particularly visual, with changes in the sense of time and space but they do not impair memory. *Cannabis Sativa* is a tall weed which is the source of marijuana. The *bharg* of India is obtained by cutting the tops of the plant and boiling or steeping them in water or milk. Another familiar preparation is *Ganja*. These are also referred to as *euphoric*.

Lysergic acid diethylamide (LSD) is the most important drug among the hallucinogens. Large doses can be fatal. Other hallucinogens which have been used widely are *mescaline* (obtained from a cactus) and *psilocybin* (obtained from a Mexican mushroom).

QUESTIONS

20.1 Write the products of benzenesulfonic acid with the following

- | | | |
|--------------------|----------------------------------|-------------------------|
| a. C_2H_5OH | b. $NaOH$ (cold) | c. $NaCN$ (aq) |
| d. Br_2, Fe | e. $NaHCO_3$ (aq) | f. dil H_2SO_4 , heat |
| g. $CH_3Cl-AlCl_3$ | h. fuming sulfuric acid and heat | |
| i. H_2O | j. $Ba(OH)_2$ | |

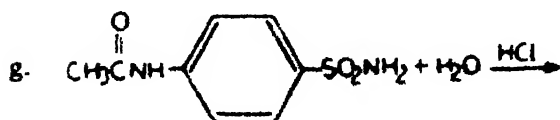
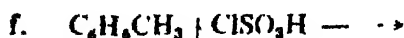
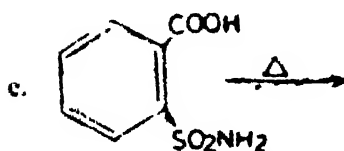
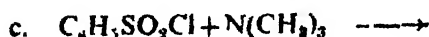
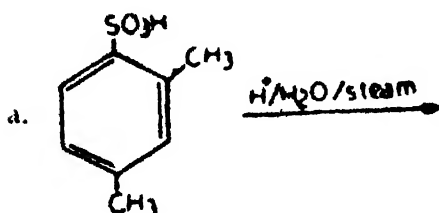
20.2 Outline the synthesis of the following, starting from benzene or toluene and any other reagent.

- a. Phenol b. *p*-Cresol c. Phenyl *p*-toluenesulfonate
 d. Resorcinol e. *p*-Bromobenzenesulfonamide

20.3 Write the structure and the name of the major product obtained from the sulfonation of the following compounds.

- a. Chlorobenzene b. Anisole c. Toluene
 d. *p*-Nitrotoluene e. *p*-Xylene f. Nitrobenzene
 g. *m*-Xylene

20.4 Complete the following reactions



20.5 A compound with molecular formula C_8H_{10} gives a single monosulfonated product B, on reacting with conc. sulfuric acid. The sodium salt of B, on fusion with sod. hydroxide and subsequent acidification yields a phenol (C). Write the structures of A, B and C.

20.6 Compound A C_7H_8 , on sulfonation with conc. sulfuric acid, yields two monosulfonated isomeric products B and C. The potassium salt of B, gives $\text{C}_7\text{H}_7\text{N}(\text{D})$ with KCN which on hydrolysis forms an acid E, $\text{C}_7\text{H}_5\text{O}_2$. Identify the compounds A to E.

20.7 Explain how would you proceed to separate the following mixture?

- a. Aniline
- b. N – Methylbenzenesulfonamide
- c. Sulfanilamide
- d. N, N—Dimethylbenzenesulfonamide

20.8 Discuss the general methods for the preparation of aromatic sulfonic acids Explain how (a) benzene (b) phenol and (c) benzoic acid may be prepared from it.

20.9 Give one method of preparation, two properties and one use of *p*-toluenesulfonic acid.

20.10 Give an account of the sulfonating agents in organic chemistry.

20.11 How will you obtain a pure sample of benzenesulfonic acid in the laboratory? What happens when its sodium salt is (i) fused with NaOH (ii) treated with phosphorus pentachloride (iii) fused with sodamide and (iv) the acid treated with steam under pressure?

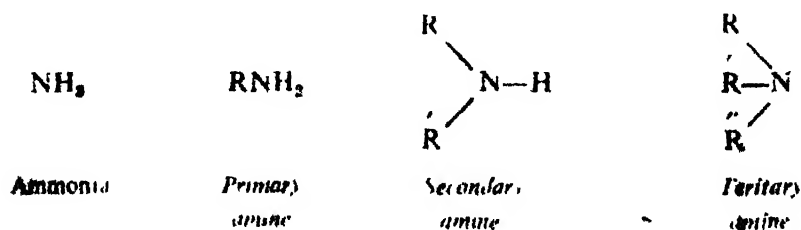
20.12 What are chemotherapeutic agents? Name some of them

Amines, Dyes and Nitro Compounds

Air contains about 78% nitrogen by volume. Molecular nitrogen is very stable and also very unreactive. Strictly speaking, organic reactions that consume molecular nitrogen are unknown but there are a number of inorganic reactions that do consume it. Molecular nitrogen is also "fixed" or converted into nitrogen containing compounds with the aid of certain bacteria. The only non-biochemical nitrogen reaction in nature is the conversion of molecular nitrogen into its oxides. Nitrogen is, however, fixed biochemically into ammonia which in turn is converted into more complex nitrogenous compounds.

Amines are nitrogen containing compounds which may be considered as derivatives of ammonia in which hydrogen atoms have been replaced by alkyl or aryl groups. The amino group is present in a number of important substances. The most significant of them probably are the amino acids. Many dyes and many medicinal agents (Benadryl, amphetamine, etc.) and alkaloids contain amino groups.

Amines are classified into three types, i.e. primary, secondary and tertiary depending on whether one, two or three hydrogen atoms of ammonia have been replaced by alkyl or aryl groups



Section A: ALIPHATIC AMINES

Aliphatic amines are those in which only the alkyl groups replace the hydrogen atoms in ammonia.

21.1 NOMENCLATURE OF ALIPHATIC AMINES

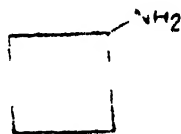
The simple amines are known by their common names which are derived by placing the suffix *--amine* at the end of the alkyl group.



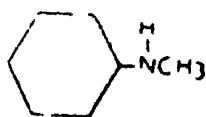
Methylamine



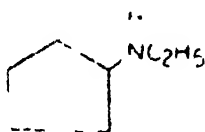
Butylamine



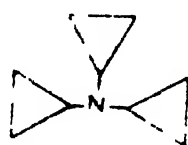
Cyclobutylamine



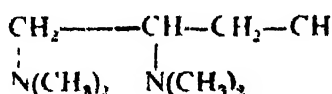
Methylcyclohexylamine



Ethylcyclopentylamine



Tricyclopropylamine

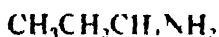


1,3 Di(dimethylamino) butane
or
1,3 bis dimethylaminobutane

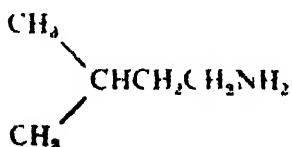
In the IUPAC system, an amine is named as a derivative of a parent hydrocarbon and the --NH_2 group is denoted by the prefix *-amino*. Numbering is needed to specify the position of the substituent



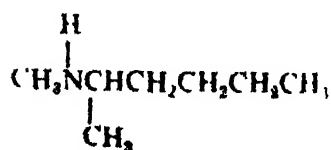
Aminomethane



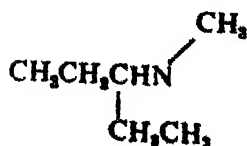
Aminopropane



3-Methyl -1- -aminobutane



2-(N-Methylamino)hexane



2-(N-ethylmethylamino)butane

21.2 PHYSICAL PROPERTIES OF ALIPHATIC AMINES

Aliphatic amines are capable of hydrogen-bond intermolecularly ($N-H\cdots N$). As a result, primary and secondary aliphatic amines possess higher boiling points than the corresponding alkanes but lower than the alcohols. The tertiary amines do not enter into hydrogen-bonding. Amines are moderately polar substances.

Gaseous and liquid amines have a noxious odor and are difficult to work with. Di- and trimethylamines are found in rotting fish and are partly responsible for its peculiar smell. High molecular weight amines and most aromatic amines do not have particularly strong odors. Aliphatic amines are considerably more basic than the aromatic amines, they also form hydrogen-bond with water and thus show significant solubility. The aromatic amines on the other hand, are slightly less soluble.

Table 21.1 Physical Constants of Amines

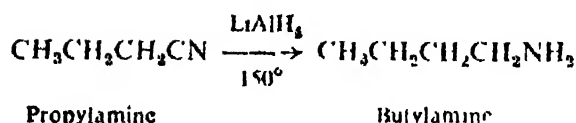
Amine	m.p. ($^{\circ}C$)	b.p. ($^{\circ}C$)
Methylamine	92	-7.5
Dimethylamine	96	9.5
Trimethylamine	-117	3
Ethylamine	-80	17
Diethylamine	39	55
Triethylamine	115	89
<i>n</i> -Propylamine	-85	49
<i>n</i> -Butylamine	-104	63
<i>iso</i> -Butylamine	-50	78
<i>sec</i> -Butylamine	-67	66
<i>t</i> -Butylamine		134
Cyclohexylamine		185
Ethanediamine	8	117

21.3 PREPARATION OF ALIPHATIC AMINES

The aliphatic amines as a class are obtained by reduction processes.

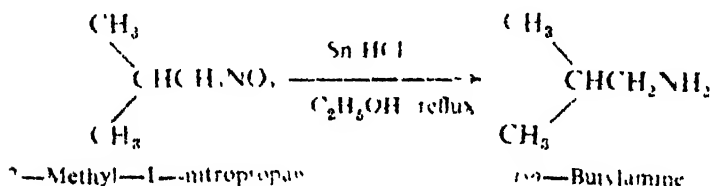
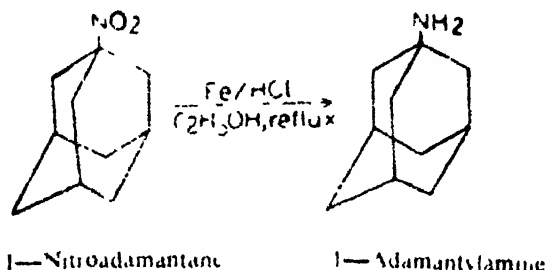
Primary Amines (1°)

1. *Reduction of Nitriles*. Nitriles may be reduced to primary amines by chemical means. Lithium aluminum hydride or hydrogenation can effect this conversion.



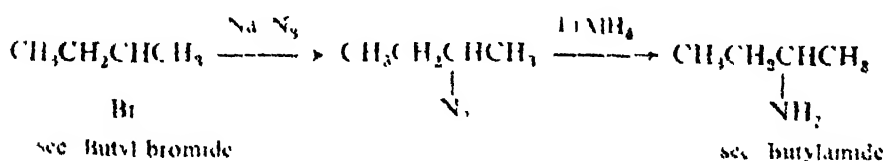
The reaction involves the addition of 2 moles of H_2 across the triple bond at the $-\text{CN}$ group.

2. *Reduction of Nitroalkanes* Like the cyanides, nitro compounds are reduced in the presence of iron powder and aqueous acid solution :

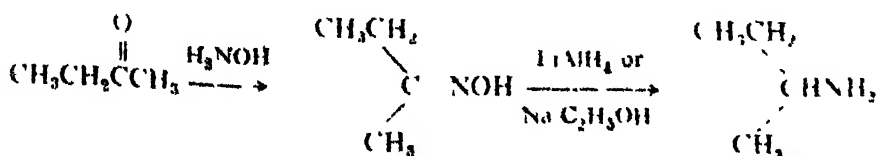


This method however is more suitable for the preparation of aromatic amines.

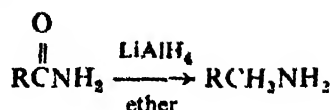
3. *Reduction of Alkylazides* Azides may be obtained by the $\text{S}_{\text{N}}2$ displacement of alkyl halide with Na^+N_3^- . These on reduction with LiAlH_4 furnish amines.



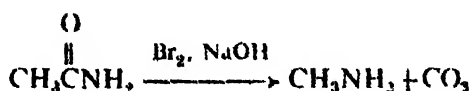
4. *Reduction of Oximes*: Oximes are prepared by the condensation of ketones with hydroxylamine hydrochloride. The resultant product is then reduced with LiAlH_4 or with $\text{Na/C}_2\text{H}_5\text{OH}$.



Amides are similarly reduced with LiAlH_4 to amines.

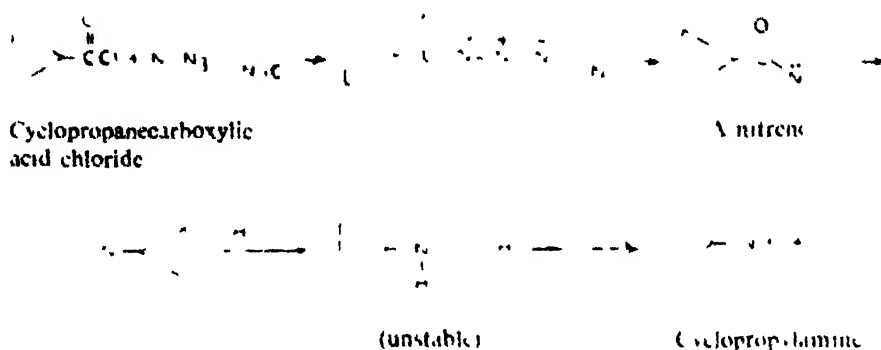


5. *Hofmann and Curtius Reactions*: In the Hofmann reaction an amide is treated with bromine and NaOH to form an amine.

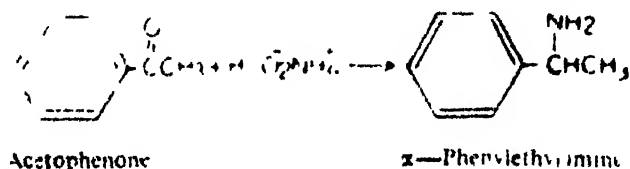


The mechanism of the reaction has been described in Chapter 19.

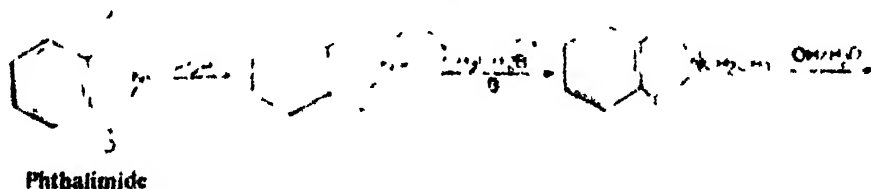
The Curtius reaction involves heating of an acid azide to give an amine *via* a nitrene.

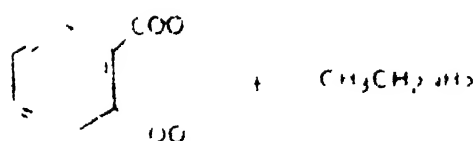


6. *The Leukart Reaction*: In this method a ketone is heated at 180–200° with ammonium formate to produce an amine.



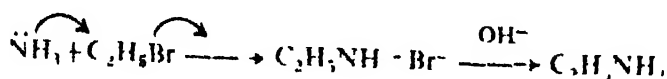
7. *The Gabriel Synthesis* This method gives pure primary amines in good yields. Phthalimide is first prepared from phthalic acid and ammonia; such imides have acidic properties because the resulting anion can be stabilized by resonance. The phthalimide anion has nucleophilic properties and can displace a halide ion from an alkyl halide. The product, an N-





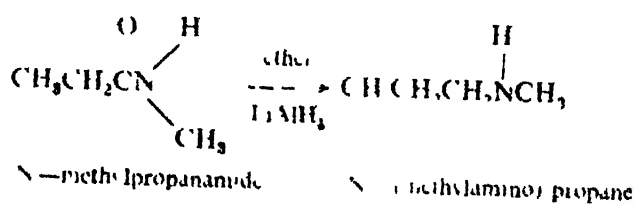
Ethylamine

alkylphthalimide, on hydrolysis gives the amine and phthalic acid. Salts of primary amines can be prepared from ammonia and alkyl halides by nucleophilic substitution reaction. Treatment of the resulting ammonium salts with base gives primary amines.

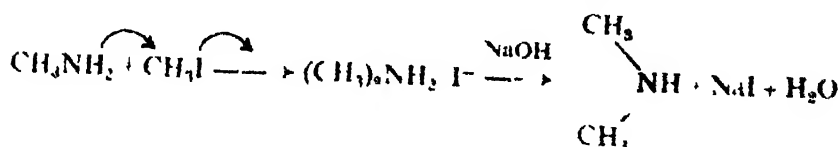


Secondary Amines (2°)

1. Reduction of *N*-substituted amines with LiAlH_4 gives a secondary amine.



2. Alkylation of a primary amine with an alkyl halide in molar amounts is a useful method for the synthesis of a secondary amine.



3. *Reduction of Isocyanides*: The reduction of an alkyl isocyanide forms a secondary amine containing one methyl group.

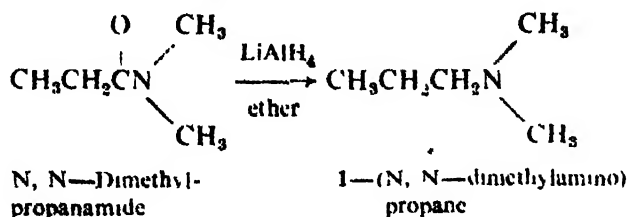


Tertiary Amines (3°)

1. Complete alkylation of amines or ammonia gives a low yield of tertiary amines.

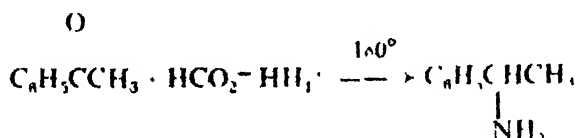
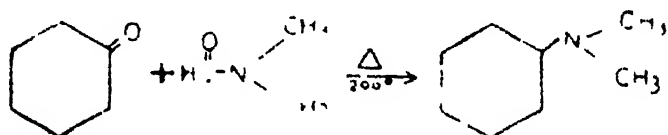


2. **Reduction of Disubstituted Amides :** Dialkyl substituted amides on reduction with LiAlH_4 form tertiary amines



Reduction may alternatively be carried out using diborane in THF.

3. **The Leukart Reaction:** This reaction involves heating a ketone at $180^\circ\text{--}200^\circ\text{C}$ with N, N—dimethylformamide. This reaction can be used to prepare primary or secondary amines as well

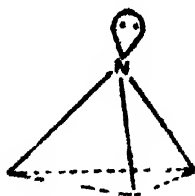


In summary, the following four methods may be employed for the preparation of either of the three types of amines

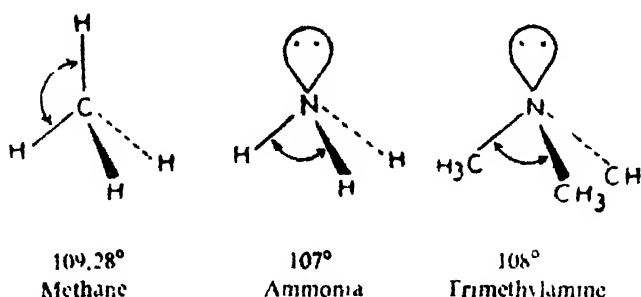
- (i) Reduction of amides
- (ii) Alkylation of ammonia or amines
- (iii) Leukart reaction
- (iv) Reductive amination (See p. 571)

21.4 GEOMETRY AND BASICITY OF AMINES

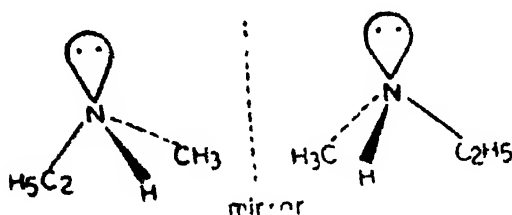
The ammonia molecule is pyramidal, with nitrogen at the apex of a pyramid and a hydrogen atom at each corner of its triangular base as shown below:



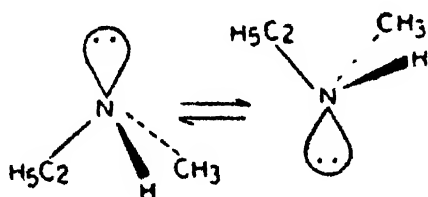
The nitrogen atom in ammonia is sp^3 hybridized, i.e., it forms sp^3-s σ -bonds with hydrogen and the unshared electron pair is placed in the fourth sp^3 orbital. The bond angles in methane, ammonia and trimethylamine are shown below :



Because of the tetrahedral nature of the nitrogen atom in amines, they might appear to be asymmetric and thus resolvable into enantiomers. But



such an optical isomerism has never been observed. This is attributed to the fact that one form is transferred into the other rapidly due to a low energy barrier of only 6 kcal/mole, and thus the two forms are interconvertible. For quaternary ammonium salts, on the other hand, in which four groups



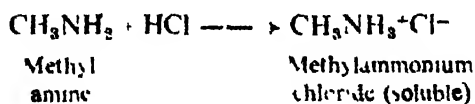
are attached to nitrogen are tetrahedral because all four sp^3 orbitals are used to form bonds, and such an inversion is not possible. Therefore, in quaternary ammonium salts, a nitrogen atom linked to four different groups should show optical isomerism and optical activity.

Table 21.2 pK_b Values of Amines

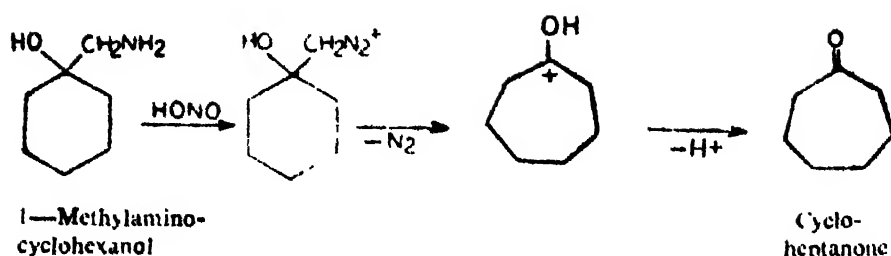
Amine	pK_b	Amine	pK_b
NH_3	4.76		
CH_3NH_2	3.38	$(\text{C}_2\text{H}_5)_2\text{NH}$	3.06
$\begin{array}{c} \text{CH}_3 \\ \diagdown \\ \text{NH} \\ \diagup \\ \text{CH}_3 \end{array}$	3.25	$(\text{C}_4\text{H}_9)_3\text{N}$	3.45
$(\text{CH}_3)_4\text{N}$	4.28	$\begin{array}{c} \text{CH}_3 \\ \diagdown \\ \text{CHNH} \\ \diagup \\ \text{CH}_3 \end{array}$	3.27
$\text{C}_2\text{H}_5\text{NH}_2$	3.46	$(\text{CH}_3)_2\text{CNH}_2$	4.21

are more basic than ammonia because of the electron-donating properties of the alkyl groups make electrons more available on the nitrogen atom for donation. An opposite effect of basicity is observed if electron-withdrawing groups are bonded to the nitrogen atom. Another important point to be noticed here is the fact that $(\text{CH}_3)_3\text{N}$ is less basic than either $(\text{CH}_3)_2\text{NH}$ or CH_3NH_2 . This is explained in terms of steric hindrance of the alkyl groups which prevent the donation of the electron pair on the nitrogen atom.

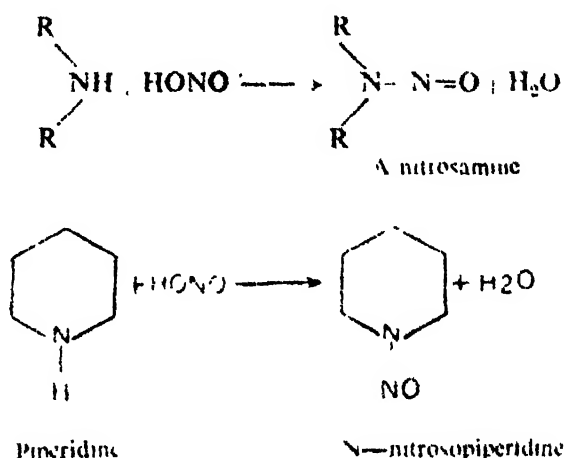
The basic properties enable amines to form salts with acids and since these salts are ionic, they are usually soluble in water.



This property of amines is employed in separating them from other compounds. For instance, consider a mixture of phenol (b.p. 182°), acetophenone (b.p. 202°) and aniline (b.p. 184°). The components cannot be easily separated by fractional distillation from the mixture. The separation can be

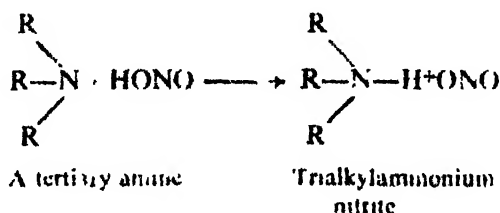


Secondary amines react to form N-nitrosamines, which separate from the reaction mixture as yellow oily liquids.



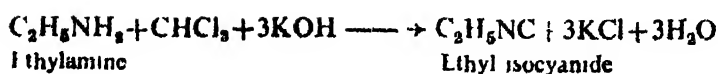
Nitrosamines are poisonous compounds and believed to be carcinogenic, i.e. cancer causing agents.

Tertiary amines simply dissolve in nitrous acid forming a salt.

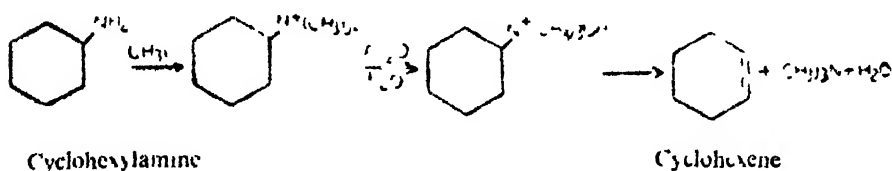


Nitrous acid is a useful reagent to determine whether an amine is 1°, 2° or 3°.

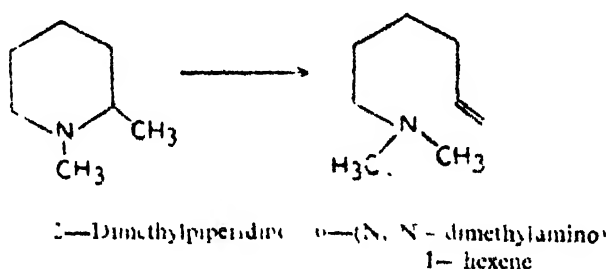
5. Carbylamine Reaction: Aliphatic as well as aromatic primary amines react with chloroform and potassium hydroxide solution to yield isocyanides. This reaction is often used as a test for the identification of a primary amine.



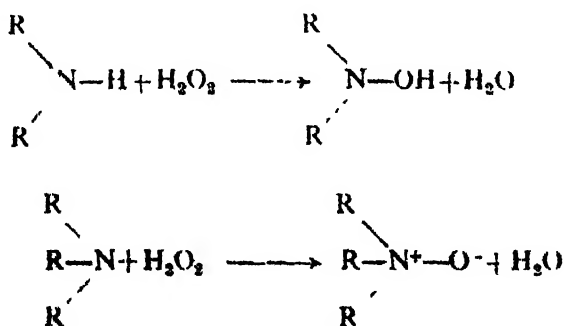
6. **Hofmann Degradation:** A quaternary ammonium hydroxide results from the reaction of a quaternary ammonium halide and moist Ag_2O . This on heating strongly suffers an elimination to give an alkene; this process is known as *Hofmann degradation*.



This is an E_2 elimination in which the hydroxide ion functions as the base. The structure of the final olefinic product assists in the establishment of the structure of the original amine. Similarly 1,2-dimethylpiperidine gives the following product

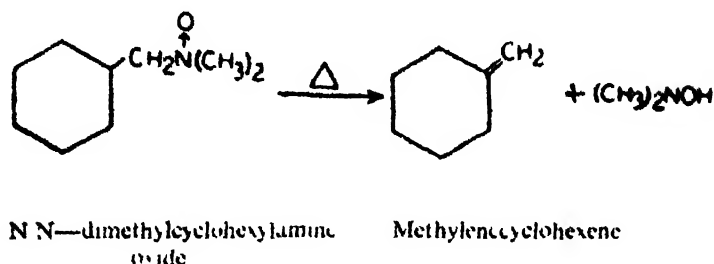


7. **Oxidation:** Amine are oxidized with ease in the presence of hydrogen peroxide, H_2O_2 or per acids. A primary amine is oxidized easily to give a mixture of products, a secondary amine yields the hydroxylation product, while a tertiary amine gives an oxide as the sole product.



An asymmetric amine oxide can be separated into optical isomers.

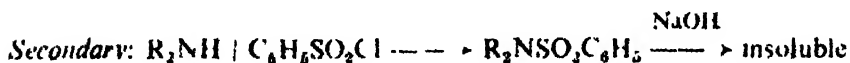
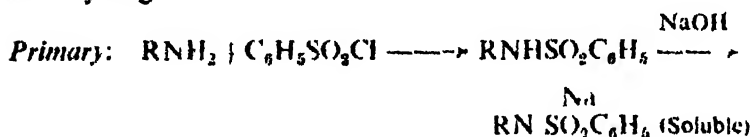
The tertiary amine oxide containing a β -hydrogen atom, on heating forms an alkene and the reaction is known as the *Cope reaction*.



21.6 IDENTIFICATION OF AMINES

A qualitative test for the identification of amines has already been stated, i.e., the formation of water soluble salt with dil hydrochloric acid. After the unknown compound has been identified as an amine, it is important to classify it into a primary, secondary or tertiary amine. The following two tests may be used.

1. *Hinsberg Test*: This test involves the reaction of an amine with benzenesulfonyl chloride in the presence of aqueous sodium hydroxide. Primary and secondary amines form a sulfonamide whereas a tertiary amine does not undergo any reaction because it does not possess a replaceable hydrogen atom.



The sulfonamide of the primary amine contains an acidic proton and can form a salt with sodium hydroxide which is soluble. The secondary amine sulfonamide lacks this proton and is thus insoluble in NaOH.

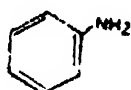
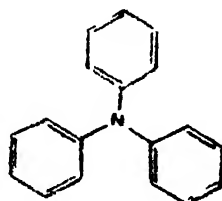
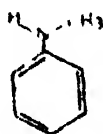
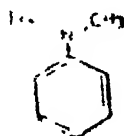
In practice, to distinguish among primary, secondary and tertiary amines, the unknown amine is shaken in a test tube with benzenesulfonyl chloride and dil. sodium hydroxide solution. A primary amine is present if a clear solution is obtained. If an insoluble organic layer remains it can be either due to a secondary or tertiary amine, because a secondary amine forms an insoluble sulfonamide whereas a tertiary amine does not react. These two can be distinguished by acidifying the mixture with dilute hydrochloric acid.

If the layer disappears it is a tertiary amine because it will form a water soluble salt but separation of an insoluble compound, a neutral sulfonamide, indicates a secondary amine.

(ii) *Reaction with HNO_2* : This reaction has been discussed already in Section (21.5).

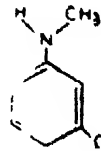
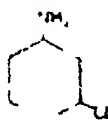
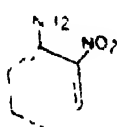
Section B: ARYL AMINES

The amino group in aryl amines is bonded directly to the aromatic nucleus. These are aryl derivatives of ammonia. Like aliphatic amines, they are also classified into three types

Aniline (1°)Diphenylamine (2°)Triphenylamine (3°)N-Methylaniline (2°)N,N-Dimethylaniline (3°)

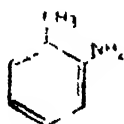
21.7 NOMENCLATURE OF ARYL AMINES

Aromatic amines are often named as derivatives of the simplest aromatic amine, i.e., aniline.

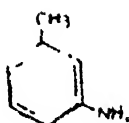


Aniline *o*-Nitroaniline *m*-Chloroaniline *p*-Bromoaniline *m*-Chloro-N-methylaniline

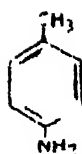
Aminotoluenes are given the special names of toluidines



o-Toluidine



m-Toluidine



p-Toluidine

21.8 PHYSICAL PROPERTIES OF ARYL AMINES

Aromatic amines are usually toxic. They possess higher boiling points than the aliphatic amines. They become colored by atmospheric oxidation. Aromatic amines also form salts with dilute hydrochloric or sulfuric acid.

21.9 PREPARATION OF ARYL AMINES

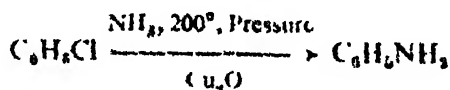
1. The first member of the arylamines, aniline, is prepared on an industrial scale by two methods.

- Reduction of nitrobenzene
- Reaction of ammonia with chlorobenzene

Nitrobenzene, in the presence of Fe and 30% hot hydrochloric acid, forms anilinium hydrochloride, which on neutralization with Na_2CO_3 regenerates aniline.

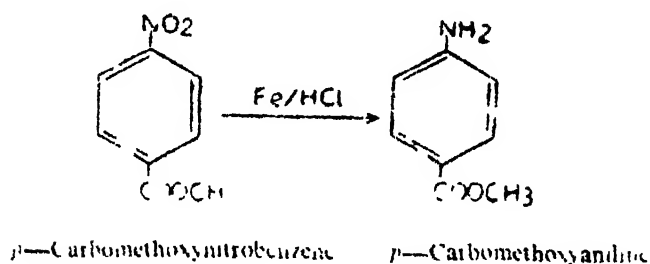
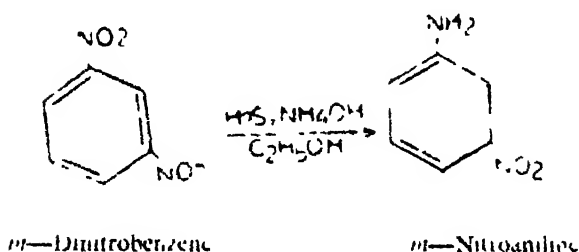
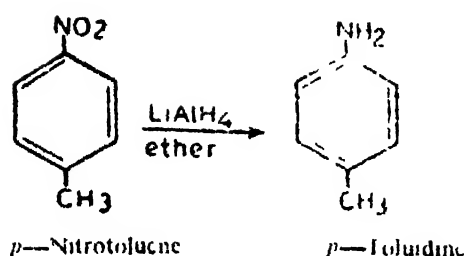


Ammonia reacts with chlorobenzene under high pressure and high temperature in the presence of a catalyst (Cu_2O), to give aniline.

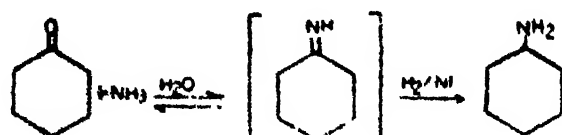
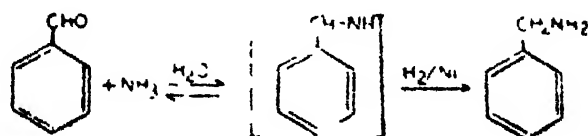


Chlorobenzene and other aryl halides do not undergo normal $\text{S}_{\text{N}}2$ displacement but halide ions can be easily replaced from aryl halides containing nitro group at the *ortho* and *para* positions.

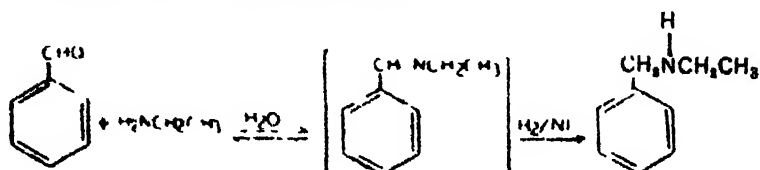
2. Aniline derivatives are prepared in the laboratory by reducing different nitro compounds. This is illustrated by the following examples.



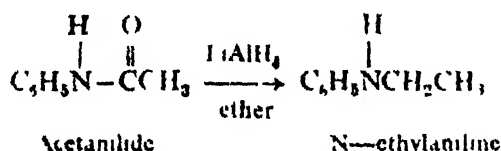
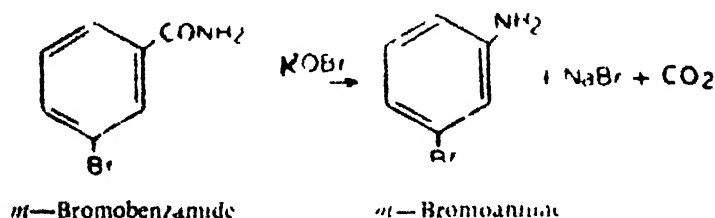
3. *Reductive Amination* Carbonyl functions are reduced rather sluggishly on catalytic hydrogenation in comparison to alkenes. But the C = N bond in imines adds hydrogen rapidly in the presence of transition-metal catalysts. Thus imines obtained on reaction of an aldehyde or ketone with ammonia or amine, on reduction yield amines. This process is called *reductive amination*. The intermediate imines are normally not isolated.



A secondary amine can be prepared through this process, using an aldehyde or ketone in the presence of a primary amine. This is illustrated for the preparation of ethylbenzylamine

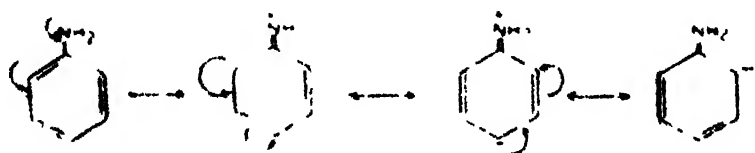


4. *Hofmann Reaction* Aromatic amides, on treatment with Br_2 , KOH give a good yield of amines



21.10 BASICITY OF ARYL AMINES

Aryl and aromatic amines are considerably less basic than aliphatic amines. The basicity of aliphatic amines is comparable to a dilute solution of sodium hydroxide and that of aromatic amines to sodium acetate. The lesser basicity of aniline compared to cyclohexylamine can be explained by the delocalization of the non-bonding electron pair on the nitrogen atom with the π -electrons of the benzene ring as shown below



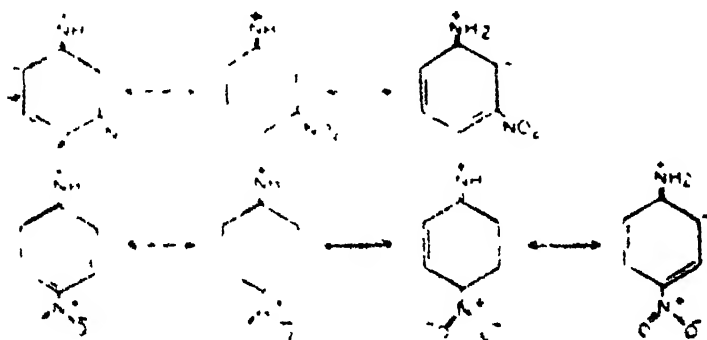
Thus the difference in basicity between the aliphatic and aromatic amines is ascribed to, for the most part, to conjugation. As a matter of fact, the additional electron pair delocalization that occurs in triphenylamine ($\text{C}_6\text{H}_5)_3\text{N}$ reduces its basicity to approximately the level of an alcohol or ether

($K_b \sim 10^{-17}$). The secondary and tertiary aromatic amines would be anticipated to still weaker because of the added steric effect to electron donation or protonation of the nitrogen atom. Presence of substituents on the benzene ring in aniline effects basicity in a predictable manner, i.e., electron-donating groups increase basicity while electron-withdrawing groups decrease basicity (Table 21.3). This happens both by inductive and resonance effects

Table 21.3 pK_a of Aromatic Amines

Aniline	4.66	<i>m</i> -Bromoaniline	3.57
<i>N</i> -methylaniline	4.80	<i>p</i> -Bromoaniline	3.86
<i>o</i> -Toluidine	4.44	<i>o</i> -Anisidine	4.52
<i>m</i> -Toluidine	4.72	<i>m</i> -Anisidine	4.23
<i>p</i> -Toluidine	5.10	<i>p</i> -Anisidine	5.34
<i>o</i> -Chloroaniline	2.65	<i>o</i> -Nitroaniline	0.26
<i>m</i> -Chloroaniline	3.50	<i>m</i> -Nitroaniline	2.47
<i>p</i> -Chloroaniline	3.99	<i>p</i> -Nitroaniline	1.0
<i>o</i> -Bromoaniline	2.53		

which act in a similar manner. Consider, for instance, *m*-nitroaniline which is more basic than the *p*-isomer. The basicity in both the compounds is reduced due to the inductive electron-withdrawing effect of the nitro group. It is, however, interesting to look into the reason for the relatively decreased basicity of *p*-nitroaniline. The various contributing structures can be written as follows:



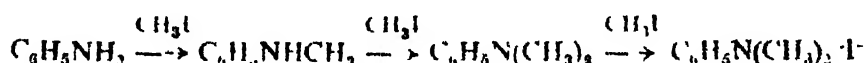
It is noticed that there is an additional contribution for the *p*-isomer, involved delocalization of the nitrogen electrons from the amino group to the *p*- NO_2 group. This is expected to cause the *p*-isomer to be a weaker base.

21.11 REACTIONS OF ARYL AMINES

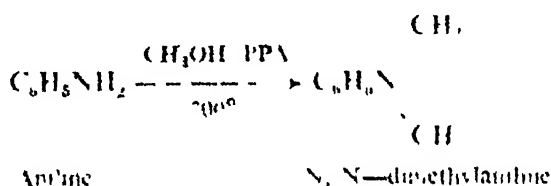
1. **Salt Formation:** Primary amines being basic form water soluble salts with mineral acids in a manner similar to aliphatic amines. The diaryl amines form insoluble salts while the tertiary amines behave as neutral compounds.



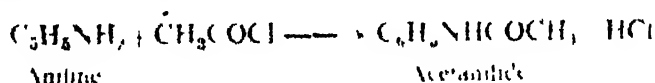
2. **Reaction with Alkyl Halides:** The hydrogen atom on the nitrogen can be successively replaced by alkyl groups to form quaternary salts.



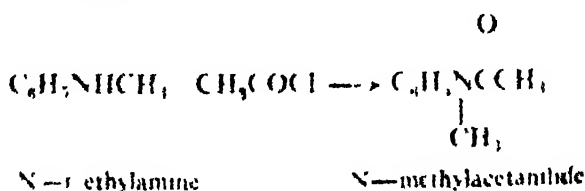
To prepare a dimethylated amine, a mixture of aniline, methanol and polyphosphoric acid may be heated



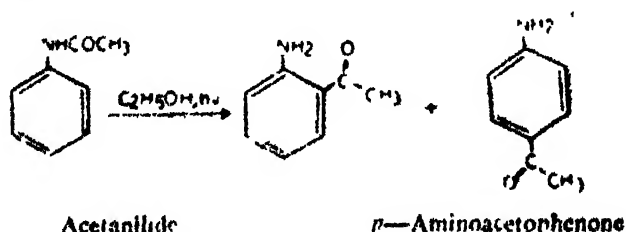
3. **Acylation:** Primary and secondary amines react with acyl halides to form H—substituted amides. Tertiary amines do not react because they have



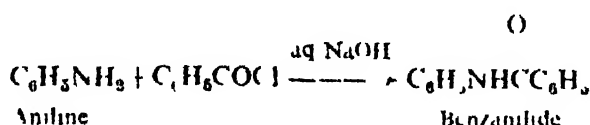
no replaceable hydrogen atom.



N—acetylated amines undergo photochemically induced Fries rearrangement to yield amino ketones

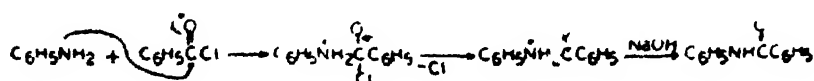


4. *N-Benzoylation*: Aromatic amines also form substituted amides in the presence of benzoyl chloride and aqueous sodium hydroxide solution. The reaction is known as *Schotten—Baumann reaction*. Sodium hydroxide is used to neutralize the HCl produced

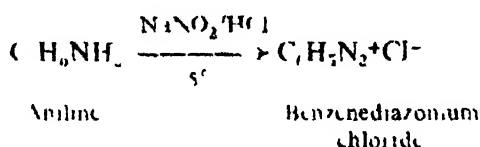


Mechanism

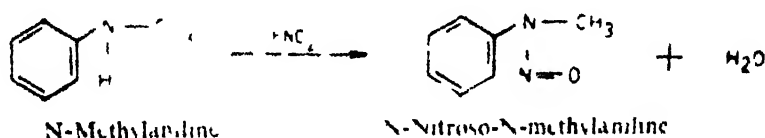
Benzoyl chloride, being an aromatic acid chloride, reacts much faster with aniline than with sodium hydroxide



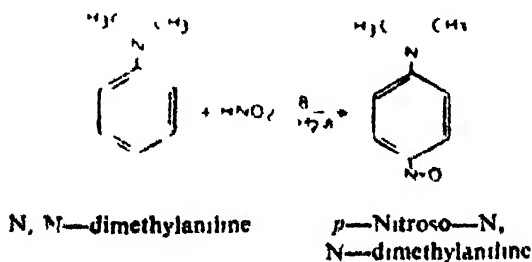
5. *Reaction with Nitrous Acid* Primary aromatic amines react with HNO_2 at a low temperature to give diazonium salts which are used as important synthetic agents (Section 21.12)

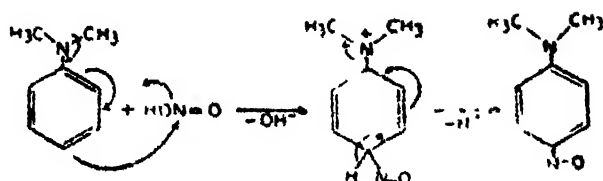


Secondary amines get nitrosated

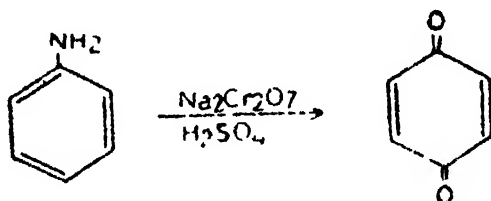


Tertiary amines lack a hydrogen atom and get nitrosated aromatic in the aromatic ring almost exclusively at the para-position

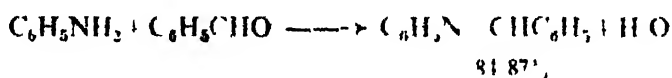


Mechanism

6. *Oxidation*: Aniline is a good source for the preparation of *p*-benzoquinone by oxidation with sodium dichromate and sulfuric acid.



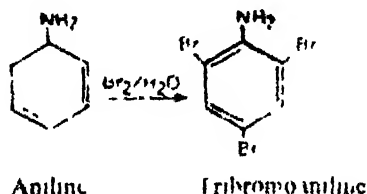
7 *Formation of Schiff's Base* Aniline condenses with an aldehyde with the loss of water to form an imine or Schiff's base. An aromatic amine forms a more stable Schiff's base than an aliphatic amine.



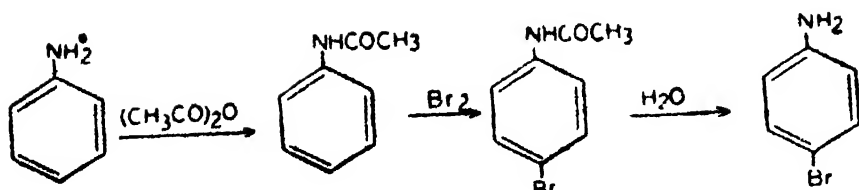
These are not important as bases but occur as intermediates in transamination and many other reactions.

8 *Ring Substitution Reactions*: The amino group is an electron-repelling group and thus activates the aromatic ring at the *ortho* and *para* positions for electrophilic substitution.

a. *Halogenation* Bromination or chlorination of aniline takes place readily and does not require the presence of a catalyst. With bromine crystalline tribromoaniline, a useful derivative of aniline, is formed. This reaction is analogous to the bromination of phenol.

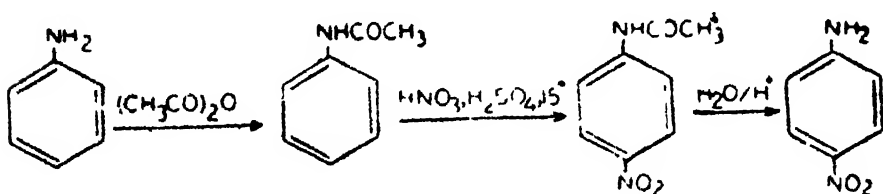


With chlorine, trichloroaniline is formed in the presence of HCl. *p*-Bromoaniline may be obtained according to the following sequence



Acylation of the amino group decreases its activating effect.

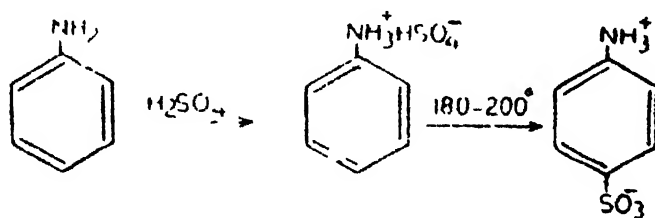
b. *Nitration*: Nitration of an amine is carried out on an acetylated amine rather than on the free amine itself. There are two reasons for this (i) The free amine is very reactive and acetylation lowers its reactivity, (ii) Free amine is very susceptible to oxidation and much of it is thus lost in the form of a tarry material.



Aniline

p-Nitroaniline

c. *Sulfonation*. The amino group itself reacts with sulfuric acid to form anilinium sulfate. The salt on heating further with sulfuric acid at a high temperature forms the *p*-isomer, i.e. sulfanilic acid. Sulfonation is



Aniline

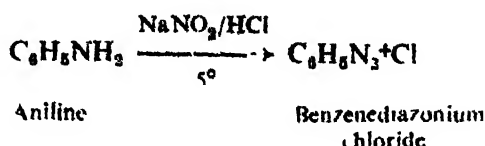
Sulfanilic acid

known to be reversible but the *p*-isomer is the most stable. Sulfanilic acid has a high melting point (300°C) and is very soluble in water but insoluble in organic solvents. This is due to its existence in a 'zwitterion' form.

21.12 DIAZONIUM SALTS

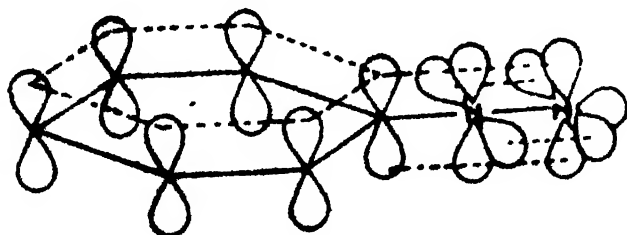
Aromatic amines undergo a unique reaction with sodium nitrite and a mineral acid to form very reactive organic compounds known as *diazonium*

salts. These salts contain a diazo (—N=N—) group and the process is known as *diazotization*.



The salts have the general formula $\text{Ar—N}^+=\text{N}^+\text{X}^-$, where X^- is an anion. The diazonium salts are unstable and explode in the dry state. Fortunately, all their useful reactions can be carried out in aqueous solution.

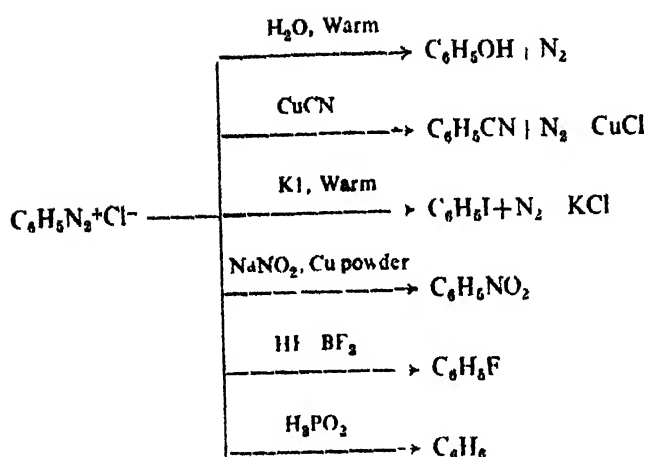
Procedure: A known weight of distilled aniline is dissolved in dil hydrochloric acid in an Erlenmeyer flask and the solution is cooled in ice. To the solution of aniline hydrochloride is added dropwise, and with constant stirring, a pre-cooled solution of sodium nitrite. The mixture is stirred continuously and the addition is regulated so that the temperature does not rise above 5°C . The reaction flask is kept immersed in an ice bath. This is the benzenediazonium chloride solution and is used as much for further reaction without isolation. The stability of the diazonium salt, in part, is due to the overlap of the orbital of the ion with that of the aromatic ring as shown below:



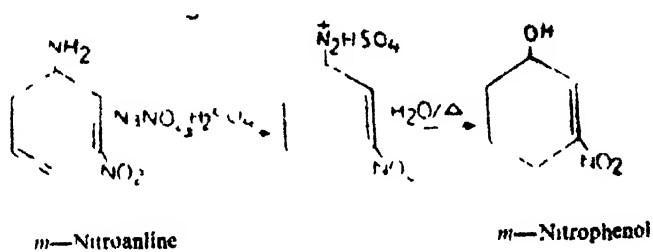
Reactions

The diazonium salts are not isolated from their aqueous solutions, instead they are treated with a particular reagent that will form the desired product. These salts function as useful organic intermediates and a large number of organic compounds can be obtained from them. Their synthetic importance can be recognized by the following reactions:

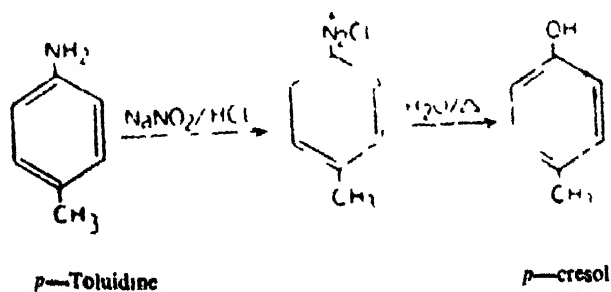
1. **Replacement of Nitrogen:** The nitrogen from the diazonium salts can be easily replaced by suitable nucleophiles.



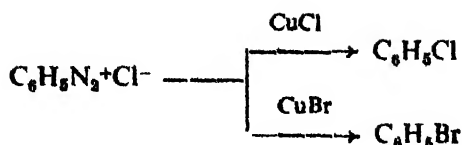
The first reaction amounts to hydrolysis of the benzenediazonium salt to form a hydroxy compound *m*-Nitrophenol, accordingly may be obtained starting from *m*-nitroaniline



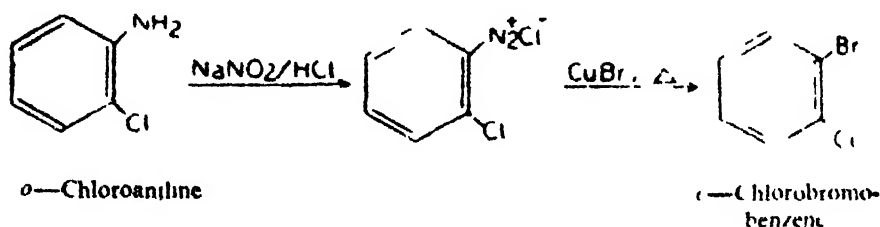
The preparation of cresols involves a similar sequence and toluidines serve as the starting material



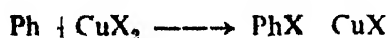
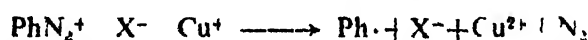
The displacement of nitrogen by the cyanide ion as well as by chloride and bromide ions is known as the *Sandmeyer reaction*. This reaction offers a



convenient method to prepare aryl halides. An example is the conversion of *o*-chloroaniline to *o*-chlorobromobenzene. An added advantage of diazonium salts is that they serve to provide satisfactory methods for the synthesis of aryl iodides and fluorides. The preparation of aryl fluorides by this method is often referred to as the *Schlemm* reaction.

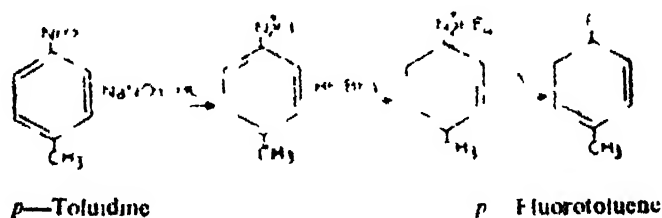


The Sandmeyer reaction occurs in two steps

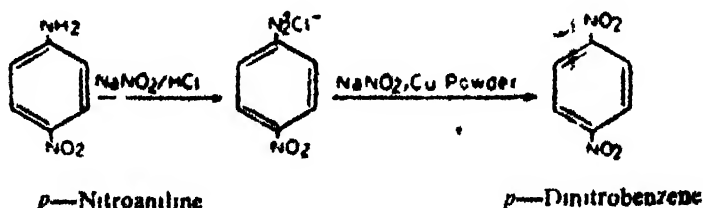


X—Br or Cl

In the first step the substrate is reduced by copper (I) ions and the second step involves a ligand transfer process leading to the product

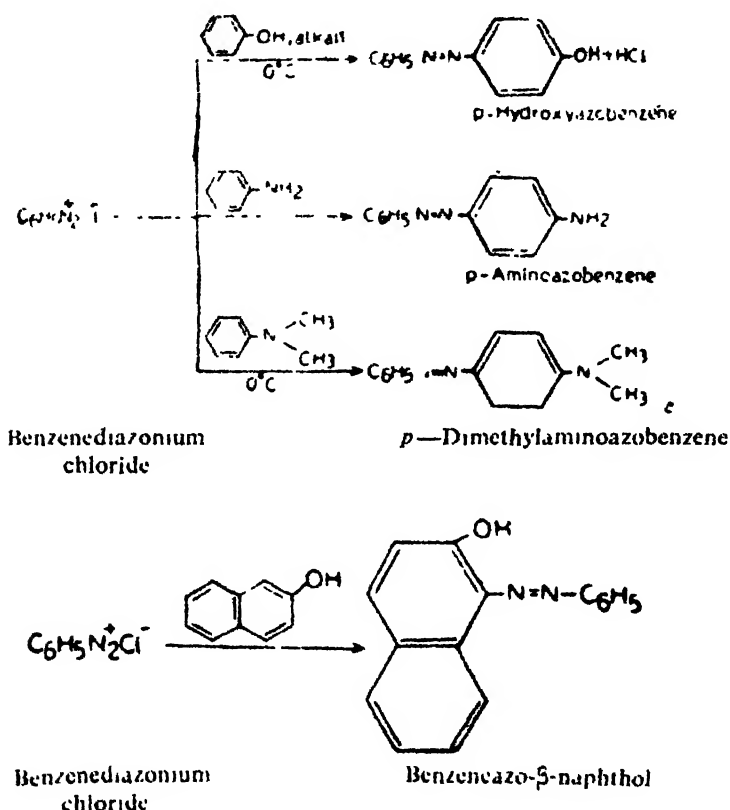


Mono- or dinitro-benzenes can also be prepared from the diazonium salts.



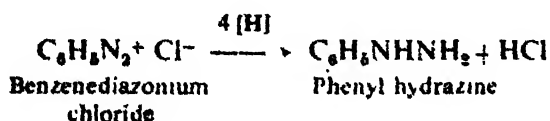
Nitrogen can be replaced by a hydrogen atom using hypophosphoric acid, H_2PO_3 to produce a hydrocarbon.

2. **Coupling Reactions:** If phenols or aromatic amines are added to an alkaline or neutral solution of a diazonium salt, a coupling reaction takes place in which the diazo group ($-\text{N}=\text{N}-$) is retained and the products are azo compounds. The aromatic ring undergoing attack by the diazonium ion must contain a strong electron-releasing group such as $-\text{OH}$, $-\text{NH}_2$, $-\text{N}(\text{CH}_3)_2$, etc.

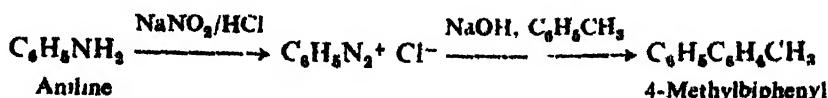


The reaction is a kind of electrophilic aromatic substitution and coupling takes place *para* to the $-\text{OH}$ or $-\text{NH}_2$ group unless this position is blocked. The azo compounds are usually colored (orange, red or yellow) and the reaction is used in the detection of primary aromatic amines. The products are useful dye-stuffs.

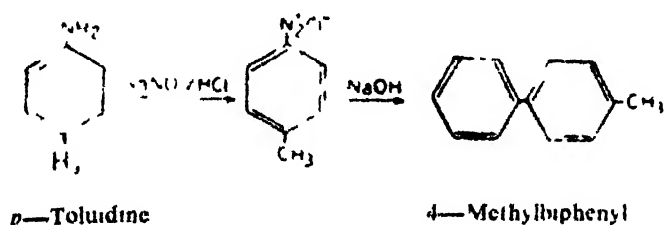
3. **Reduction:** A diazonium salt is reduced (SnCl_2/HCl), Zn dust/acetic acid, stannous chloride/HCl or sodium bisulfite to form aryl hydrazines.



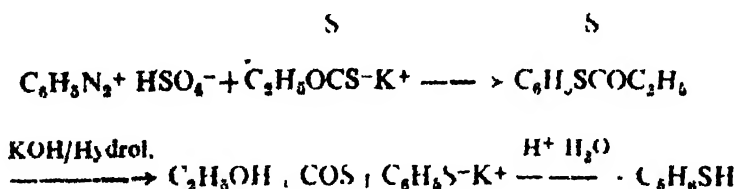
4. *Arylation*: Unsymmetrical biphenyls may be obtained by arylation of a diazonium salt. The salt is made basic and the resulting solution is stirred in the presence of an aromatic hydrocarbon.



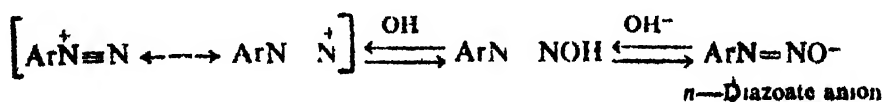
The reaction probably involves a free radical mechanism and the driving force for the reaction is the evolution of nitrogen. The above compound can also be prepared by diazotization of *p*-toluidine and subsequent reaction with benzene.



5 *Formation of Thiophenols*. Reaction of a diazonium salt with potassium ethyl xanthate and subsequent hydrolysis and acidification of potassium thiophenolate yields a thiophenol.

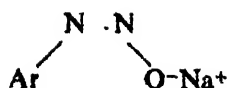


6. *Formation of Diazoates and Isodiazoates* Diazonium salts are transformed into diazoate anion on treatment with aqueous base

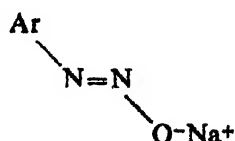


In an initial step the hydroxide ion attacks the diazonium cation to give a diazohydroxide. This being very unstable reacts with a second hydroxide ion to give the diazoate anion.

The *n*-diazoates on mixing with a strong base and heating isomerize to the more stable isodiazoates. Like the oximes, the diazoates also display geometric isomerism.



Syn-diazoate



Anti-diazoate

21.13 DYES AND DYEING

Many organic compounds are colored but all of them cannot be used as dyes. Dyes are coloring materials that can bind to the fabric or cloth they are applied to and are fast to washing and light. For a colored substance to qualify as a dye, it should contain certain types of groups which are responsible for color. Such groups are called *chromophores*. In addition, the substances must also contain groups that make them stick to the fabric. These are salt forming groups such as $-\text{NH}_2$, $-\text{COOH}$, $-\text{SO}_3\text{H}$, etc., and are called *auxochromes*. Moreover, certain groups are responsible for intensifying the colors and are known as *bathochromes*. Dyes are substantially used in the textile, food, paper, plastic and leather industries. Dyes could be either natural or synthetic, the latter types are much more important nowadays.

21.14 CLASSIFICATION OF DYES

Principal classes of dyes are the following

- | | |
|-------------------------------|--------------------------------------|
| 21.14.1 Azo dyes | 21.14.4 Fluorescein (Phthalein) dyes |
| 21.14.2 Triphenylmethane dyes | 21.14.5 Azine dyes |
| 21.14.3 Vat dyes | 21.14.6 Mordant dyes |

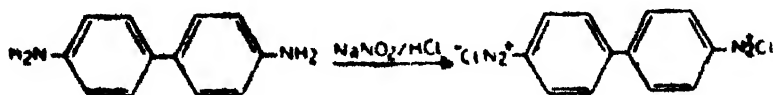
21.14.1 Azo Dyes

The azo dyes are not found in the natural materials but are instead synthesized from diazonium salts. They constitute the largest class of chemical dyestuffs. These are characterized by the presence of the diazo group. In addition they contain one or more functional groups which make them fix to the fabric and also intensify their color.

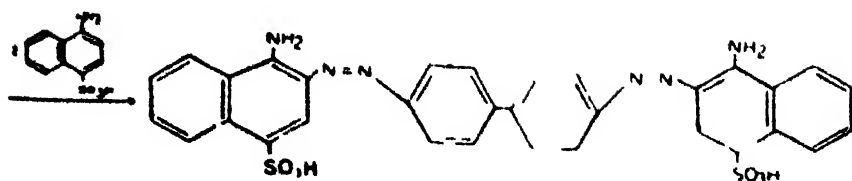
Some of the common azo dyes are given below

Congo Red

It is obtained by coupling diazotized benzidine with naphthionic acid. Since the *p*-position of naphthionic acid is blocked, coupling takes place at the position *ortho* to the amino group.



Benzidine

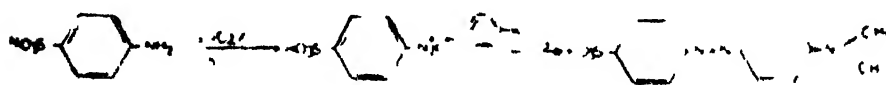


Congo red

It functions as a direct dye for cotton cloth and is also used as an indicator

Methyl Orange

Diazotized sulfanilic acid is coupled with *N,N*-dimethylaniline to obtain this dye.



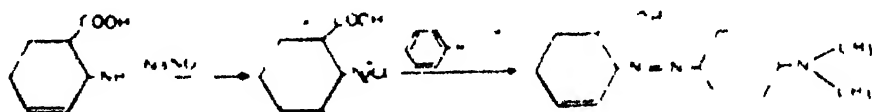
Sulfanilic acid

Methyl orange

It is employed as an indicator being orange in alkaline solution and red in acid solution

Methyl Red

Anthranilic acid is diazotized and then condensed with *N,N*-dimethylaniline to obtain methyl red.



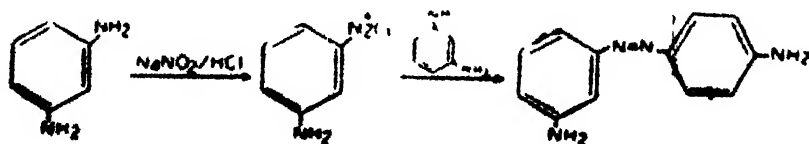
Anthranilic acid

Methyl red

It is used as an indicator

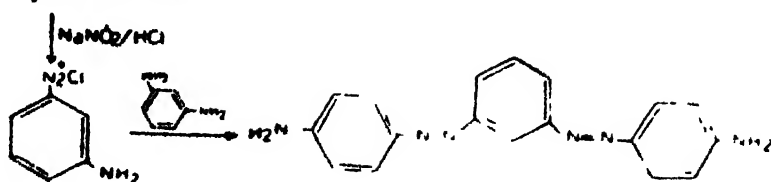
Bismarck Brown

It is a mixture of two dyes (I) and (II) obtained by the excessive diazotization of *m*-phenylenediamine and coupling with *m*-phenylenediamine



m-Phenylenediamine

(I)

***m*-Phenylenediamine**

(II)

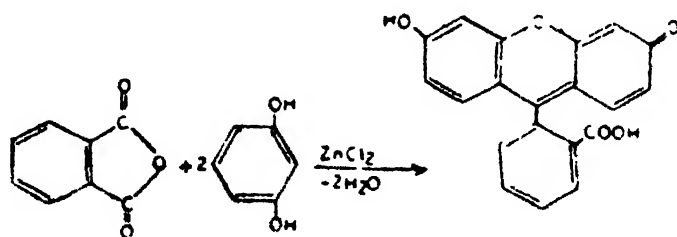
itself. It is used in shoe polishes and acts as a direct dye for dry wood.

21.14.2 Fluorescein Dyes

These dyes are derived from the condensation of phthalic anhydride with phenolic compounds

Fluorescein

It is obtained by the condensation of phthalic anhydride with resorcinol in the presence of anhydrous ZnCl_2 .



Phthalic anhydride

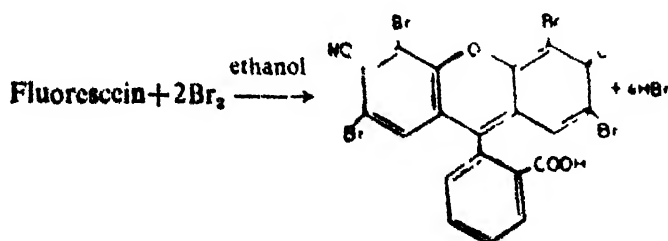
Resorcinol

Fluorescein

It is a red powder, miscible with water. It is used in organic qualitative analysis

Eosin

Bromination of fluorescein leads to eosin.



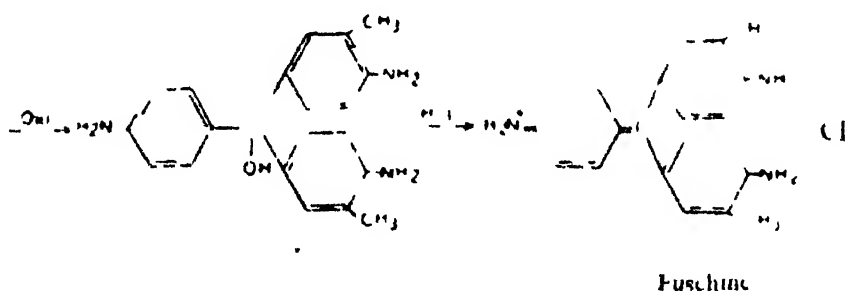
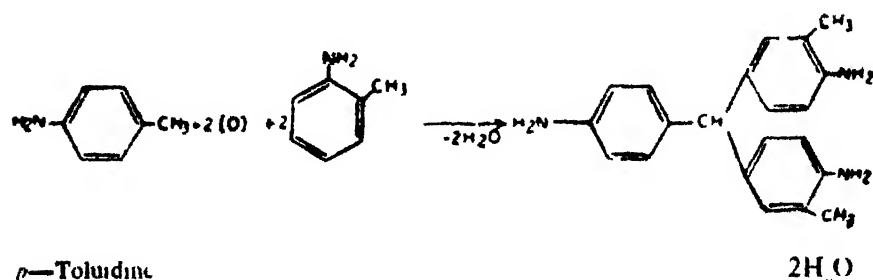
Eosin

21.143 Triphenylmethane Dyes

These are derived from the parent substance triphenylmethane and are obtained by the introduction of $-\text{NH}_2$, $-\text{NR}_2$, and $-\text{OH}$ groups into the rings of triphenylmethane

Rosaniline or Fuschine

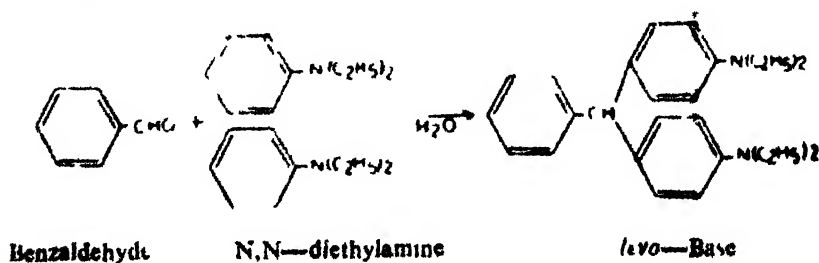
It is obtained according to the following scheme

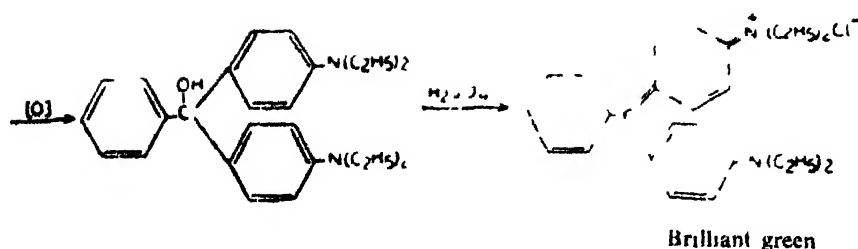


This dye is decolorized by sulfur dioxide to give what is known as the *Schiff's reagent*. The pink color is restored when shaken with an aldehyde. It dyes wood and silk.

Brilliant Green

Benzaldehyde is condensed with N,N-diethylamine to obtain the *levo*-base first, the dye is obtained by subsequent oxidation

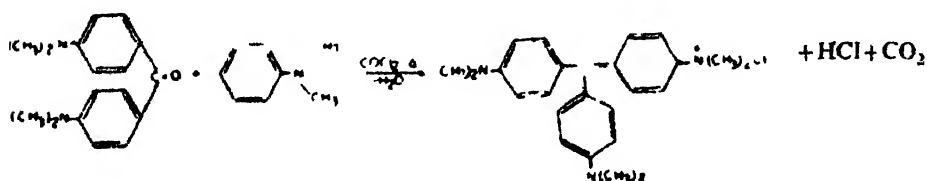




Besides its usefulness as a dye, it is also used as a powerful antiseptic

Crystal Violet

It is prepared from Michler's ketone and *N,N*-dimethylaniline as follows.

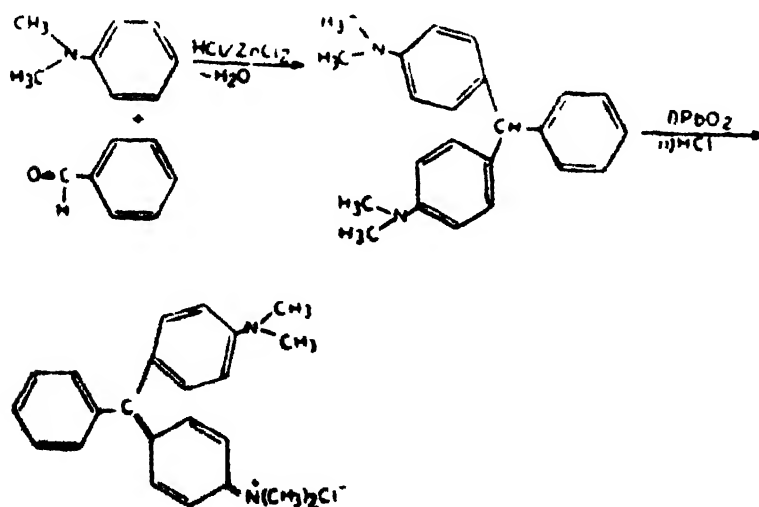


Michler's ketone

Crystal violet

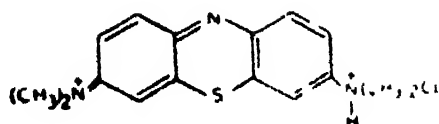
Malachite Green

It is obtained by condensing benzaldehyde with *N,N*-dimethylaniline in much the same way as brilliant green



Malachite green

21.14.4 Azine Dyes

Methylene Blue

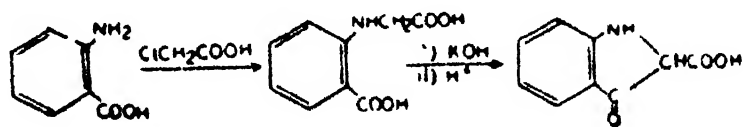
It is a derivative of thiazine and is used as a bacteriological stain

21.14.5 Vat Dyes

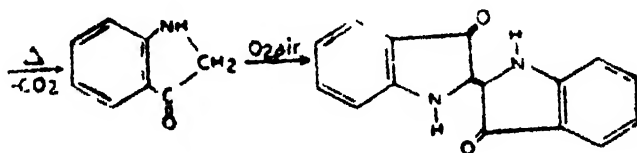
These are water insoluble colored compounds.

Indigo

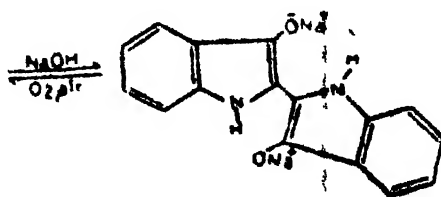
Indigo is the oldest dye used by man. It is present in the indigo plant not as such but as the compound indican a, β -glucoside which yields glucose and indoxyl on hydrolysis. Then later on oxidation by air gives indigo. It is synthesized nowadays rather than isolated from plants. It is obtained from anthranilic acid in the following steps:



Anthranilic acid



Deep blue and insoluble

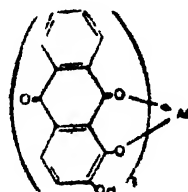
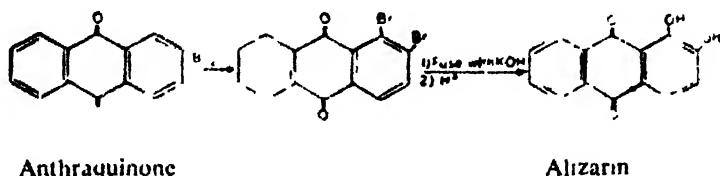


Reduced (leuco) form;
colorless but soluble

21.14.6 Mordant Dyes

Certain dyes are incapable of dyeing the fabric directly but can produce fast colors with the aid of agents known as *mordants*. Such dyes are referred to as *mordant dyes*. The mordants often include metal ions such as aluminum, iron or chromium. Alizarin and other anthraquinone dyes are important examples of this class

Alizarin



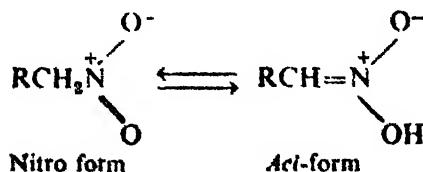
Alizarin mordanted with Al^{3+}

It is used as a dye for wool and cotton.

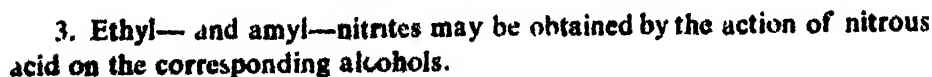
21.15 NITRO COMPOUNDS

Among the nitro compounds, nitroalkanes are rare whereas the aromatic nitro compounds are common because the latter can be prepared by nitrating benzene or its derivatives. Nitration of paraffin hydrocarbons, on the other hand, yields a mixture of products and the desired product is obtained only in a poor yield.

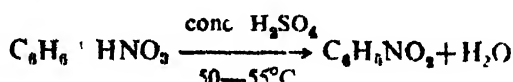
Nitroalkenes or nitroparaffins display tautomerism and, the two structures differ in the position of a mobile hydrogen atom. The methyl or the methylene hydrogens are acidic due to the presence of electron-withdrawing nitro group. The first form is known as nitro (or *pseudo acid form*) and the second as the *aci-form*



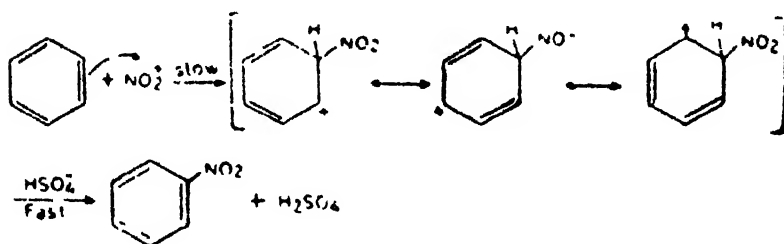
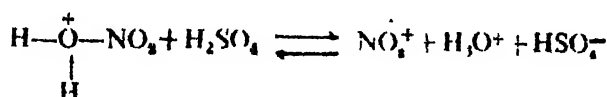
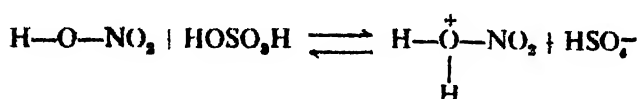
The *aci-form* can readily tautomerize to the *nitro-form*.



4. Nitrobenzene and its derivatives are prepared in the laboratory by the direct nitration of aromatic hydrocarbons. The nitrating agent of choice is a mixture of conc. nitric acid and sulfuric acid. Conc. nitric acid alone is a poor nitrating agent.



Mechanism



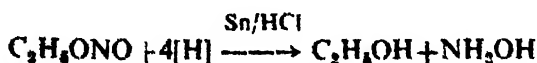
The nitronium ion reacts with the benzene ring by attacking the π -cloud and forming an arenium ion. This ion subsequently loses a proton to a base such as HSO_4^- and yields nitrobenzene. If the temperature is raised then di- and tri-nitrated products are obtained.

20.17 REACTIONS OF NITRO COMPOUNDS

1. *Reduction*: One of the most important reaction of this class of compounds is reduction. Nitroalkanes are reduced to amines.



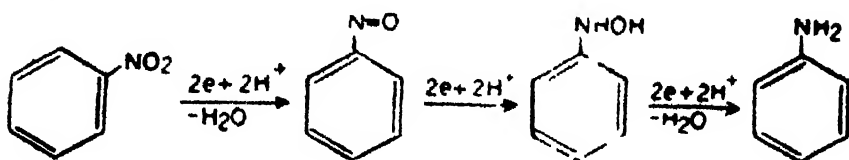
Alkyl nitrites, on the other hand, give the corresponding alcohols.



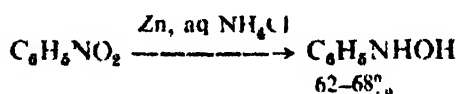
This reaction distinguishes between these two classes of compounds.

Nitrobenzene gives different products depending on the reducing agent and the medium employed.

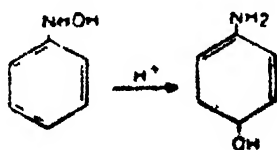
a. *Acid Medium*: With stannous chloride and conc. hydrochloric acid, aniline is formed from nitrobenzene through a series of two—electron step mechanism.



b. *Neutral Medium*: In a neutral medium, i.e., Zn in aqueous NH_4Cl , the reduction takes place upto the hydroxylamine stage.

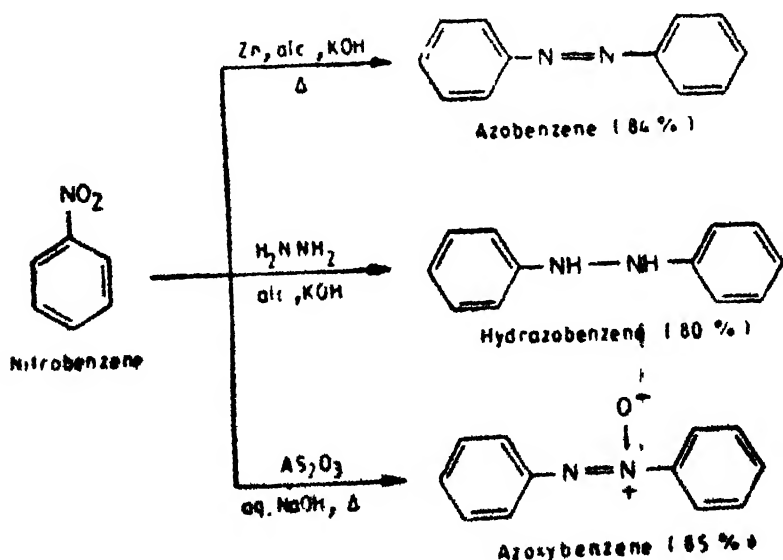


This hydroxylamine on treatment with an acid undergoes rearrangement to a *p*-aminophenol.



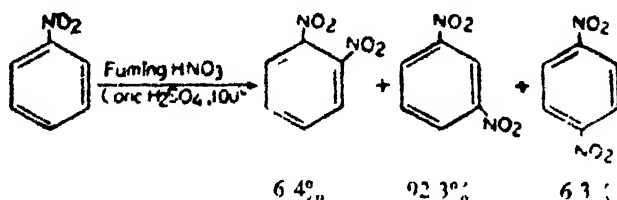
Phenyl hydroxylamine *p*-Aminophenol

c. *Basic Medium*: Bimolecular compounds are obtained on reduction of nitrobenzene in alkaline medium

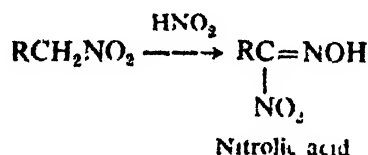


All of these products are reduced to aniline in acidic conditions.

2. **Nitration**: Further nitration of nitrobenzene is considerably more difficult because the $-\text{NO}_2$ group is an electron-withdrawing group and thus deactivates the ring towards electrophilic attack. However, using concentrated acids and higher temperature, dinitrobenzene may be obtained in 92% yield.

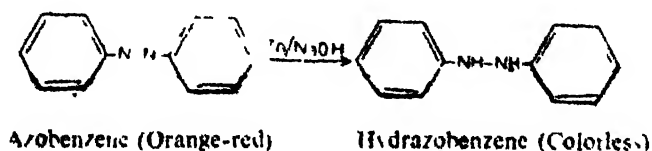


3. Nitroalkanes and alkyl nitrites may further be distinguished by the reaction with nitrous acid. A nitroalkane forms nitrolic acid while the alkyl nitrite undergoes no reaction.



21.18 HYDRAZO COMPOUNDS

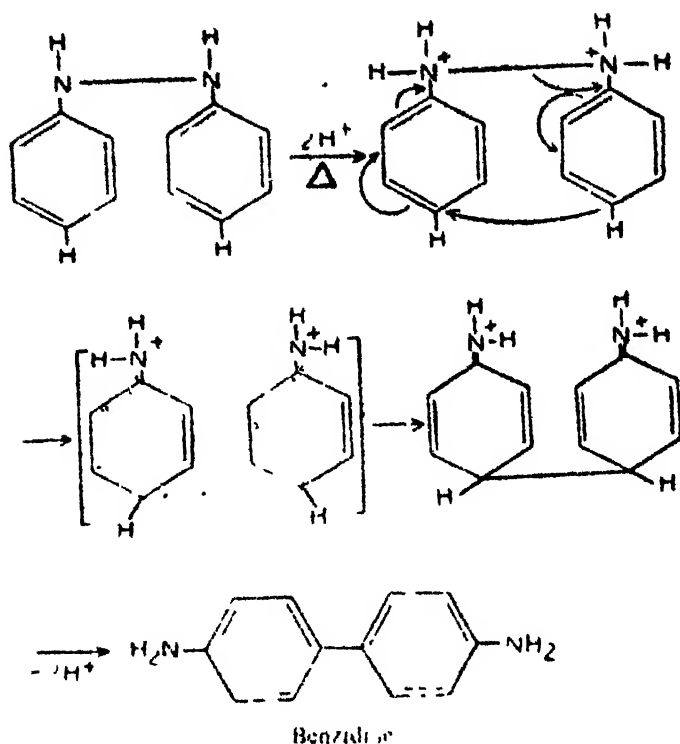
Hydrazo compounds as a class are colorless and are less important than the azo compounds which are colored. Such compounds can be obtained by mild reduction (Zn/NaOH) of azo compounds.



Symmetrical compounds, as we have seen, can be prepared by direct reduction (Zn/NaOH) of a nitro compound.

Hydroazobenzene undergo a rearrangement in strongly acidic solution to 4,4'-diaminobiphenyl, commonly called as benzidine. The reaction is, thus, known as the *benzidine rearrangement*.

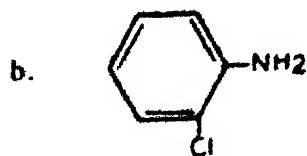
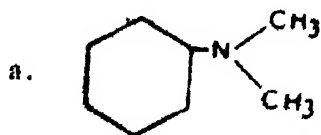
The mechanism involves the diprotonated salt, formation of a bond between the para positions of the two rings and simultaneous breaking of the $\text{N}-\text{N}$ bond.

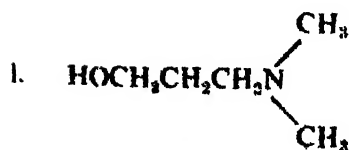
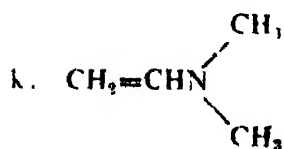
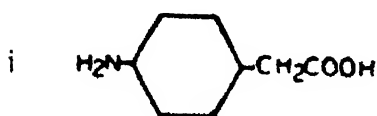
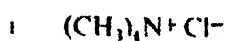
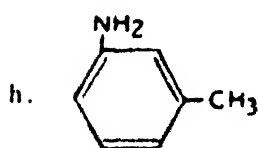
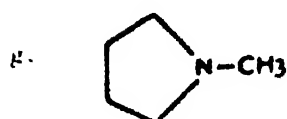
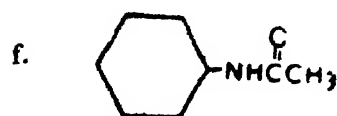
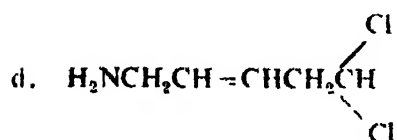
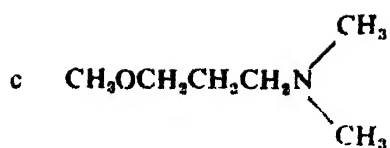


If a mixture of two hydrazobenzenes are heated in acid, only two benzidines are formed and no cross-product results. This shows that the reaction must be intramolecular. Benzidine is an important intermediate used, for example, to make direct cotton dyes.

QUESTIONS

21.1 Name the following compounds.





21.2 Discuss the basicity of cyclohexylamine and aniline.

21.3 Make the following conversions.

- a. *iso*-Butyric acid to isobutylamine
- b. Nitrobenzene to benzoic acid
- c. Aniline to *p*-bromoaniline
- d. Ethylamine to ethyl alcohol
- e. *N,N*-Dimethyl-4-pentene to 1,4-pentadiene
- f. Aniline to *s*-tribromoaniline
- g. Propene to isopropylamine
- h. Ethyl chloride to *n*-propylamine
- i. Aniline to sulfanilamide
- j. Cyclohexanone to cyclohexylamine

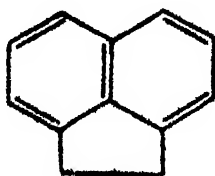
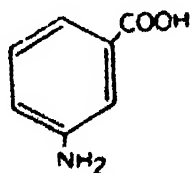
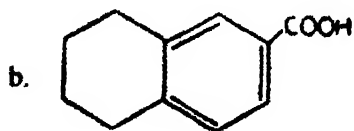
21.4 Describe the reactions of *n*-butylamine with each of the following.

- a. Benzenesulfonyl chloride + NaOH
- b. Acetyl chloride
- c. Excess methyl bromide, then Ag₂O and heat
- d. Nitrous acid
- e. H₂SO₄
- f. Dil NaOH
- g. Chlorobenzene
- h. Ethylene oxide

21.5 Is ClNH₂ a stronger or weaker base than ammonia? Discuss21.6 Write the structural formulas and names for all the amines of the formula C₄H₁₁N.

21.7 How will you proceed to separate a mixture consisting of

- a. *o*-toluidine, toluene and *p*-chlorotoluene;



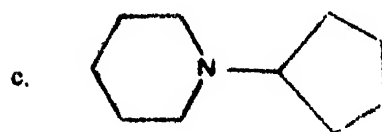
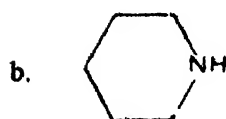
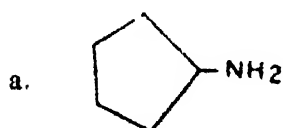
21.8 Write equations for the reaction of benzenediazonium sulfate with the following reagents:

- a. CuCl
- b. H_3PO_3
- c. KI
- d. *p*-Cresol
- e. CuCN
- f. Hot dil H_2SO_4
- g. HF , BF_3
- h. *m*-Phenylenediamine

21.9 Offer explanations for the following observations:

- a. Methylethyl *n*-propylamine cannot be resolved into its optical isomers.
- b. Methyl alcohol is less basic than methylamine.
- c. Dimethylamine is more basic than trimethylamine.
- d. The sulfonamide of a secondary amine is insoluble in NaOH .
- e. Acetanilide reacts with bromine moderately than does aniline.
- f. The reaction of nitrous acid with a secondary amine stops at the nitrosamine stage.
- g. It is not desirable to nitrate aniline directly to prepare nitroanilines.

21.10 What product(s) would be obtained from each when subjected to Hofmann degradation?



21.11 What products would be obtained by the reduction of:

- a. Methyl cyanide
- b. *iso*-Propyl cyanide
- c. Methyl *iso*-cyanide
- d. *iso*-Propyl *iso*-cyanide

21.12 Show how would you distinguish between the following pairs:

- a. Aniline and cyclohexylamine
- b. Propylamine and Methylethylamine
- c. Aniline and acetanilide
- d. Aniline hydrochloride and *o*-chloroaniline
- e. N-Methylaniline and toluidine
- f. 2, 4, 6-Trinitroaniline and *o*-toluidine
- g. Aniline and phenol

21.13 An unknown amine undergoes no reaction with nitrous acid. Its hydrochloride contains 32.4% of chlorine. What are the names and the structure of the amine?

21.14 An unknown amine A with benzenesulfonyl chloride yields a derivative which dissolves in alkali. Compound A on reaction with nitrous acid gives an alcohol B which responds to the haloform reaction. Hydrochloride of A contains 37.2% of chlorine. Write structures of A and B.

21.15 Bring out the differences in the properties of amines and amides.

21.16 An aromatic compound contains 69.4% carbon and 5.8% hydrogen. A sample of 0.303 g of this compound was analyzed for nitrogen by the Kjeldahl's method. The ammonia evolved was absorbed in 50 ml of 0.5 M sulfuric acid. The excess acid required 25 ml of 0.1 M sodium hydroxide for neutralization. Determine the molecular formula of the compound if its molecular weight is 121.

21.17 Write a short note on azo dyes.

21.18 Give the preparation and uses of the following.

- | | | |
|------------------|-------------------|--------------------|
| a. Fluorescein | b. Congo red | c. Malachite green |
| d. Methyl orange | e. Bismarck brown | f. Rosaniline. |

21.19 What is meant by diazotization? Describe the method used for the laboratory preparation of benzenediazonium sulfate. Explain, giving examples what happens when benzenediazonium chloride is made to react with:

- a. NaNO_2 and Cu powder
- b. Stannous chloride dissolved in conc. HCl
- c. Aqueous solution of KI

- 21.20 Outline the methods for the preparation of aliphatic primary amines. How are 1°, 2°, 3° amines distinguished and separated from one another?
- 21.21 Describe the preparation of phenylhydrazine. How can you convert it into:
 - a. Aniline
 - b. Antipyrine
- 21.22
 - a. How is aniline prepared on a large scale?
 - b. What products are obtained when nitrobenzene is reduced under different conditions? Give the necessary equations.
- 21.23 Define primary, secondary and tertiary amines. How are they distinguished and separated from a mixture. By suitable examples give the important features which influence the basic strengths of organic bases.
- 21.24 Why are amines more basic than alcohols?
- 21.25
 - a. What is the diazo reaction? How is the aqueous solution of benzenediazonium chloride obtained?
 - b. How will you convert benzenediazonium chloride into (a) benzene, (b) benzoic acid, (c) phenyl hydrazine.
- 21.26 An organic compound $C_4H_9I(A)$ reacts with silver nitrite to give mostly $C_4H_9O_2N(B)$. Compound B does not dissolve in alkali and also has no reaction with nitrous acid. Reduction of B, gives another compound C, which can also be obtained from A and potassium phthalimide. Compound C, reacts with nitrous acid to give a tertiary alcohol $C_4H_{10}O(D)$. Identify the compounds A, B, C and D stating the reaction involved.
- 21.27 How do you account for the effect of substituents on the basicity of aromatic amines?
- 21.28 How is benzenediazonium chloride prepared? Discuss its synthetic importance.
- 21.29 Describe the preparation and uses of phenolphthalein and malachite green.
- 21.30 What are amines? How may primary, secondary and tertiary amines be separated? Give the structural formulae and names of isomeric amines of molecular formula $C_4H_{11}N$.
- 21.31 Give the reaction of HNO_3 with the following:
 - a. aniline
 - b. N—methylamine
 - c. N, N—dimethylamine

21.32 Consider: *o*-toluidine, ethylamine, butylamine and pentamethylene diamine.

- a. Which would be made by reduction of butanonitrile?
- b. Which would react with HCl in the ratio of one mole of the compound and two moles of HCl?
- c. Which would be converted into a diazonium salt?
- d. Which would be among the products of the reaction of chloroethane and ammonia?

21.33 Which of the two amines, *N,N*-dimethylaniline or 2, 6-dimethylaniline will couple with benzene diazonium chloride? Give reasons for your answer.

Organometallic Compounds

Organometallic compounds are those in which a metal atom is linked directly to an organic radical, $R-M$. Such bonds have a high degree of ionic character $R^{\delta-} M^{\delta+}$ because metals are electropositive in nature and the carbon atom is sufficiently electronegative. This class of compounds is named by prefixing the name of the metal with the organic radical and the name is written as one word. Some examples are listed below :

CH_3Li	$(CH_3)_3Al$	$(CH_3CH_2)_2Zn$	$(CH_3CH_2)_2B$
Methyl lithium	Trimethylaluminum	Diethylzinc	Diethylcarbon
$(CH_3)_4Si$	$(C_2H_5)_2Cd$	C_6H_5Li	$(C_6H_5)_3CNa$
Tetramethylsilicon	Diethylcadmium	Phenyllithium	Triphenylsodium

In compounds of the type $RMgX$, known as Grignard reagents, the valencies of the metal are not all used in bonding to carbon but include bonds to some inorganic atoms also. The compounds are named as organic derivatives of the corresponding inorganic salts.

CH_3MgBr	C_2H_5MgCl	C_6H_5MgBr	$C_6H_5CH_2MgCl$
Methylmagnesium bromide	Ethylmagnesium chloride	Phenylmagnesium bromide	Benzylmagnesium chloride

Most of the organometallic compounds are liquids and soluble in organic solvents. They react readily with moisture and oxygen. Great care is, therefore, needed while working with these substances. Many of these compounds are normally not purified but are prepared and used as such in solution, in organic synthesis.

22.1 GRIGNARD REAGENTS

Organometallic compounds with the general formula, $RMgX$, are known as *Grignard reagents* after Victor Grignard, a Nobel prize winner (1912) in chemistry. These reagents are highly reactive and have proved to be of great utility in organic synthesis. Grignard reagents can be prepared conveniently in the apparatus shown in Fig. 22 1. It consists of a three-necked

flask equipped with a mechanical stirrer, an efficient water condenser and a dropping funnel.

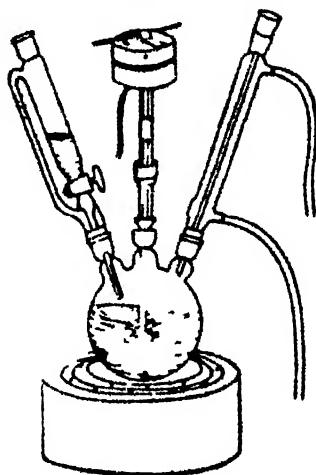
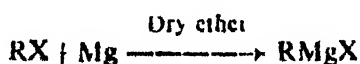


Fig. 22.1 Assembly for Grignard reaction

The reaction is usually carried out by treating magnesium turnings with an organic halide in ether

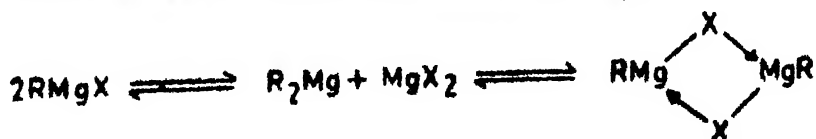


where R is an alkyl or aryl radical and X may be Cl, Br or I

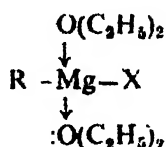
The organomagnesium halide is formed by insertion of magnesium between carbon and the halogen. The alkyl halide may be primary or secondary while tertiary ones are less soluble because of steric and electronic considerations. The R group should not contain a group bearing an active hydrogen atom such as $-\text{COOH}$, $\text{C}\equiv\text{CH}$, OH , NH_2 , etc. The reactivity among the halides follows the order $\text{RI} > \text{RBr} > \text{RCl}$, but chlorides are normally used because of their easy availability. Organomagnesium fluorides are not known yet.

22.2 STRUCTURE OF GRIGNARD REAGENTS

The structure of Grignard reagent has been a subject of much investigation by various groups of workers. Grignard himself suggested that the reagent could be represented as RMgX . Subsequently it was believed that the dimeric structure shown below is the most important which is in equilibrium with dialkylmagnesium compound and magnesium dihalide.



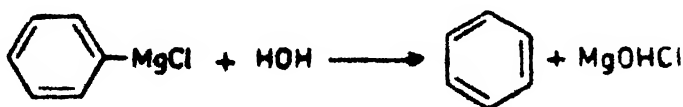
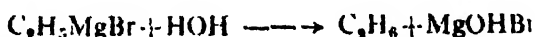
X-ray diffraction studies have revealed that the two ether molecules are also tightly bound to magnesium in RMgX .



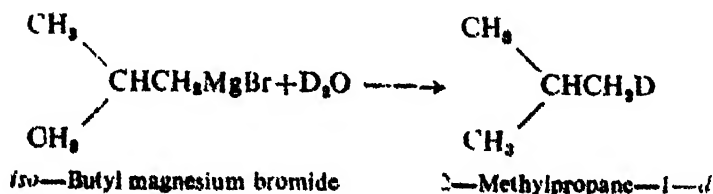
22.3 REACTIONS OF GRIGNARD REAGENTS

Grignard reagents are colorless and non-stable solids. These are prepared fresh for each synthesis and are not isolated but used as such in ethereal solution. The reagents contain a carbon magnesium bond. Since magnesium has a very low electronegativity, the carbon atom bonded to it has a high concentration of negative charge, i.e., $\text{CH}_3\text{CH}_2^-\text{MgBr}^{++}$. Because of this negative charge, the carbon atom has a high affinity for hydrogen and will react even with weak acids such as water, ammonia, phenols and carboxylic acids. Grignard reagents are not only strong bases, but are also powerful nucleophiles. These reagents are important intermediates in organic syntheses.

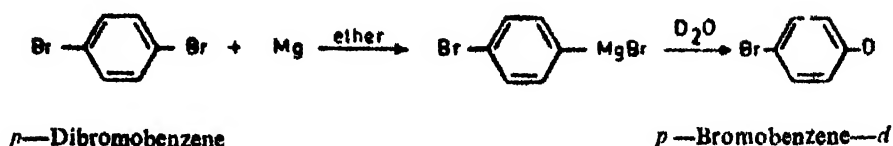
1. *Reaction with Water:* Water reacts readily with Grignard reagents and thus provide an excellent method for the preparation of certain hydrocarbons.



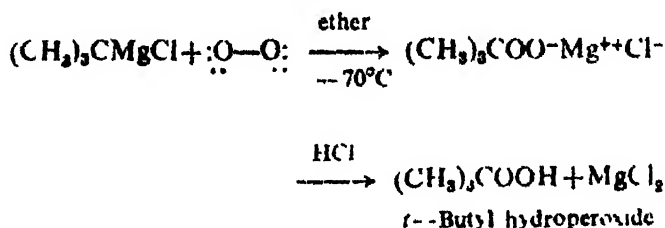
The reagents similarly react with alcohols and acids. With deuterium oxide (D_2O), a hydrocarbon containing a deuterium atom is formed.



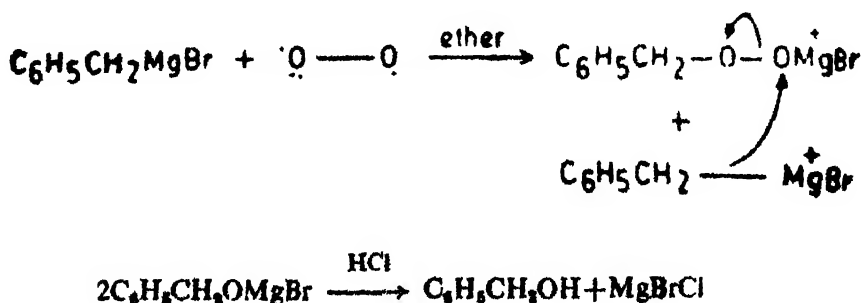
This reaction is often used as a way to introduce deuterium into organic molecules.



2. *Reaction with Oxygen:* Grignard reagents react with molecular oxygen at low temperature to form hydroperoxides, or compounds containing the $-\text{O}-\text{O}-\text{H}$ bond. Oxygen molecules contain two unpaired electrons which become paired during the first reaction.

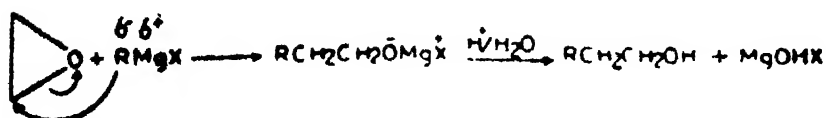
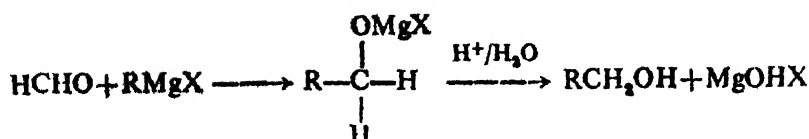


If an excess of Grignard reagent is present, then it reacts with the hydroperoxide intermediate to form alcohol.



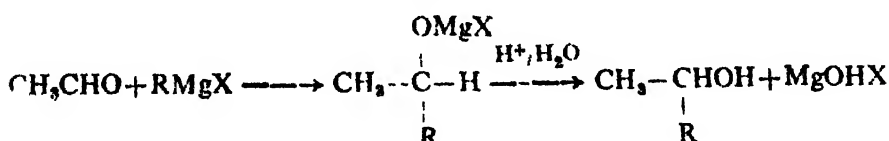
3. *Reaction with Carbonyl Compounds and Ethylene Oxide:* Grignard reagents readily add on to a carbonyl group because of the polar nature of the reagent. Using appropriate carbonyl compounds the reaction is useful for the preparation of alcohols. In each case, magnesium is transferred from carbon to a more electronegative element.

1°. A primary alcohol is obtained by reacting a Grignard reagent with formaldehyde or ethylene oxide with subsequent hydrolysis. In the case of ethylene oxide, (oxirane), the carbon chain in the product is extended by two carbon atoms.

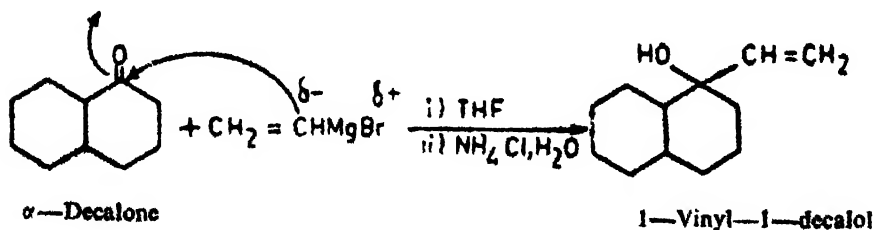
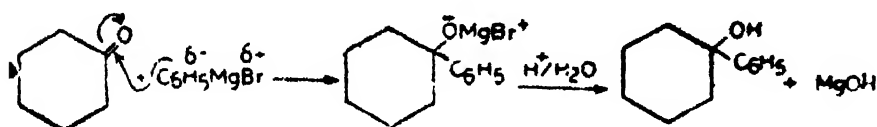
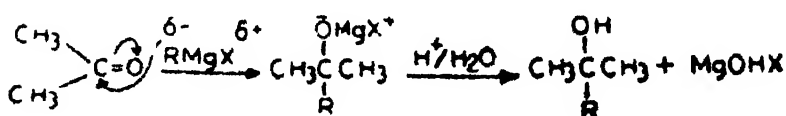


Because of the large angle strain in the small oxirane ring causes it to portray carbonyl group characteristic.

2°. A secondary alcohol results on addition of a Grignard reagent to an aldehyde, other than formaldehyde.



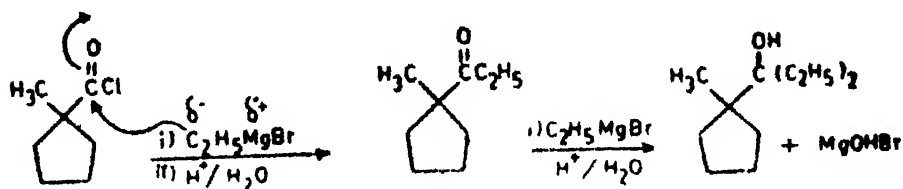
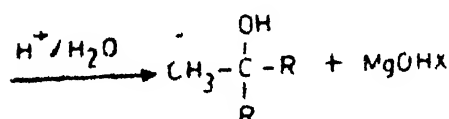
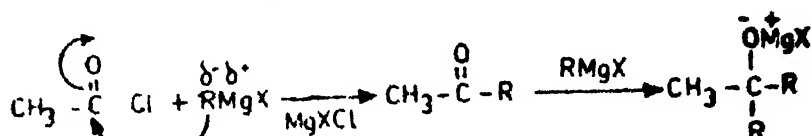
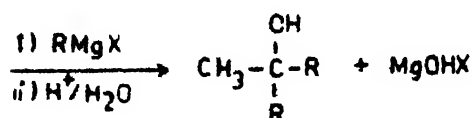
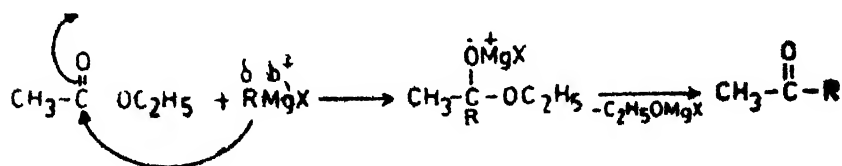
3°. A tertiary alcohol is obtained on addition of a Grignard reagent to a ketone.



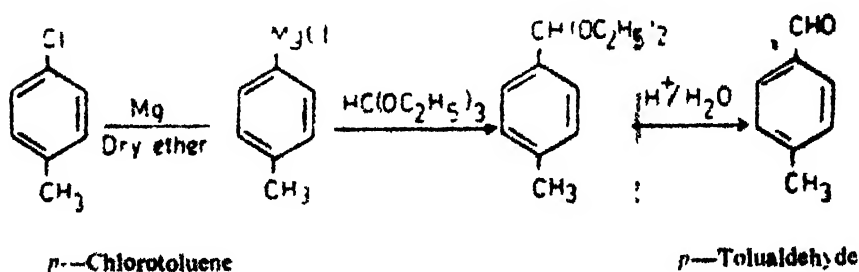
The groups in the above reactions can be varied as desired.

4. *Reaction with Esters and Acyl Chlorides:* Both these reagents usually combine with two moles of Grignard reagent to give a tertiary alcohol as the final product. The intermediate complex is unstable and decomposes

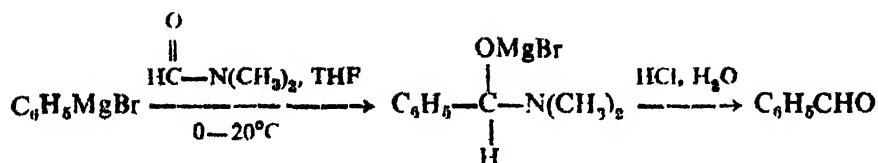
rapidly to form ketone initially. This combines again with a second mole of Grignard reagent to form an alcohol. Grignard reagents are more reactive towards ketones than esters and acid chlorides



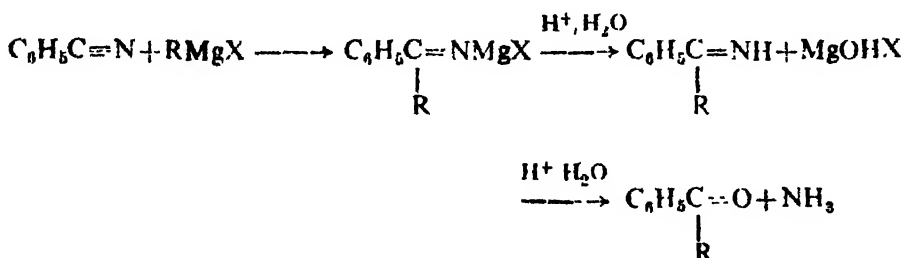
5 Reaction with ortho Esters Both aliphatic and aromatic Grignard reagents react with the ortho esters to yield the corresponding aldehydes



Aldehydes may also be prepared from Grignard reagent by treatment with N, N—dimethyl formamide and subsequent hydrolysis of the complex

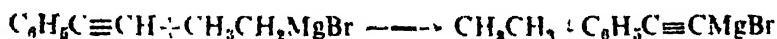


6. *Reaction with Nitriles:* A useful ketone synthesis consists of adding of a Grignard reagent to a nitrile group followed by hydrolysis, of the resulting aldimine.

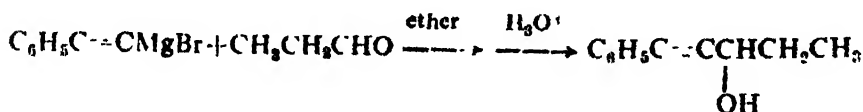


R can be varied as desired.

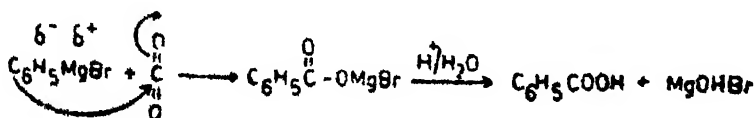
7. *Acetylenic Exchange:* Since an acetylenic hydrogen is acidic, a Grignard reagent reacts with it to give a hydrocarbon and an alkynyl Grignard reagent.

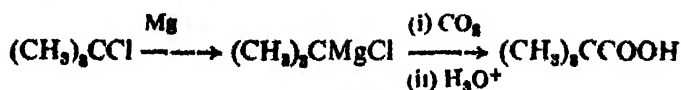


The resulting reagent can react with other organic compounds and thus offers a method for lengthening the carbon chain.

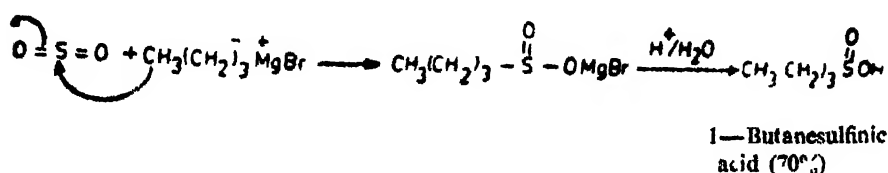


8. *Carbonation:* Aromatic carboxylic acids can be prepared by carbonation of a Grignard reagent followed by hydrolysis. Solid carbon dioxide, commonly known as *dry ice* is employed for this purpose. Carbon dioxide can be solidified under pressure at -78°C . In the above reaction the carboxyl group of carbon dioxide is subject to nucleophilic attack by Grignard reagents.

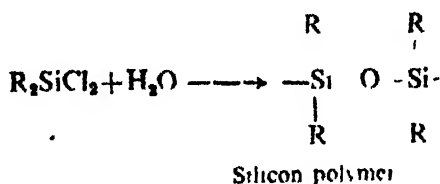
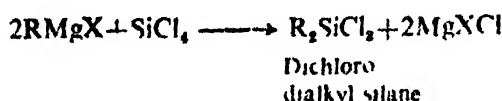




9. *Reaction with Sulfur Dioxide:* Sulfur dioxide is a good electrophile and reacts with Grignard reagents to form magnesium sulfinates which on acid hydrolysis give sulfonic acids.

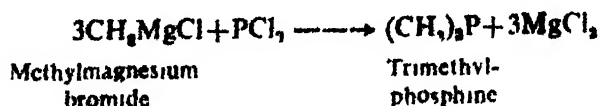


10. *Reaction with Silicon Tetrachloride:* A Grignard reagent reacts with silicon tetrachloride and the product on hydrolysis forms silicon polymer.

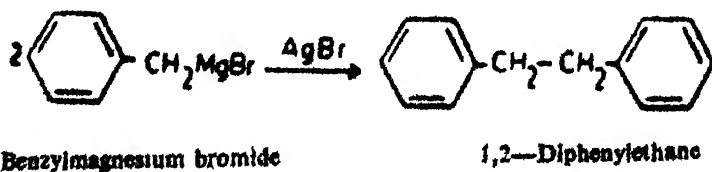


These polymers are used as high temperature lubricants in polishes and in automobiles.

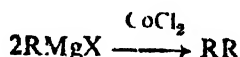
11. *Reaction with Phosphorus Trichloride:* A trialkyl phosphine is obtained on reacting a Grignard reagent with PCl_3 .



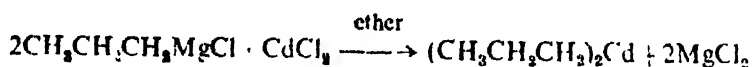
12. *Coupling Reaction:* A Grignard reagent reacts with silver bromide to give a high yield of the coupled products.



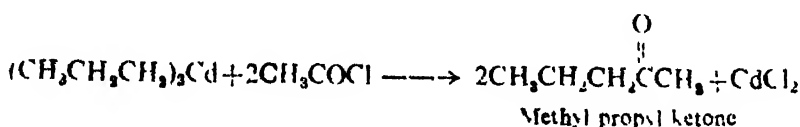
The reaction probably proceeds through a free radical pathway. Coupling also takes place by the addition of cobaltous chloride to a Grignard reagent. It is also considered to proceed through a free radical pathway.



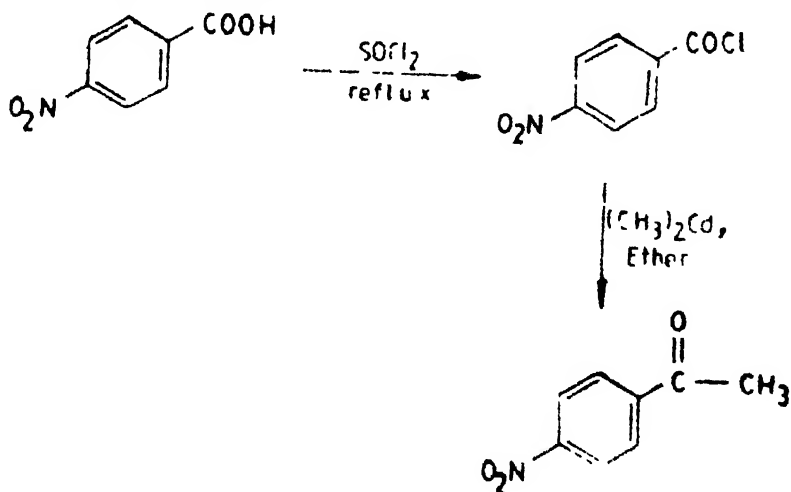
13. *Reaction with Cadmium Chloride:* A Grignard reagent readily reacts with cadmium chloride to form the heavy metal derivative, i.e., an organocadmium compound and magnesium chloride



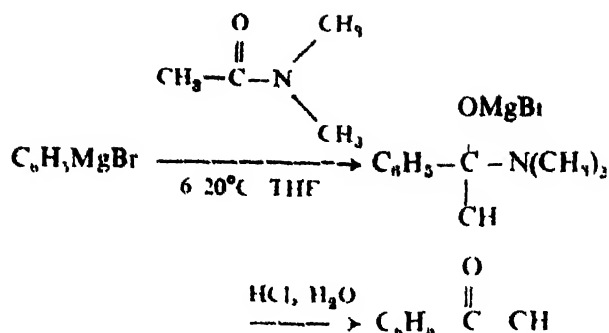
The organocadmium reagents are sufficiently nucleophilic to react with acyl halides. Thus the reaction of an organocadmium with an acyl halide is an important method for the preparation of ketones.



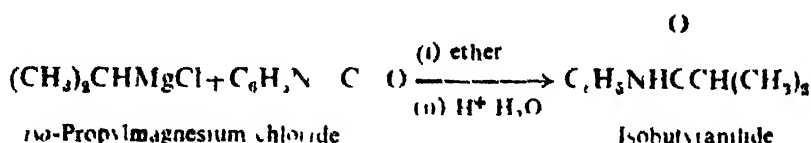
The cadmium reagents are useful because they are too unreactive to add to the by-product ketone (as the Grignard reagent adds in the case of esters and acid chlorides) and thus the reaction is stopped at the ketone stage. This procedure is also useful for the preparation of ketones containing a NO_2 substituent on a benzene ring



Another method of preparing ketones involves a reaction between Grignard reagent and *N,N*-dimethylacetamide. The intermediate complex on acid hydrolysis yields the ketone



14 Isocyanates react with Grignard reagents to give after hydrolysis, N-substituted amides

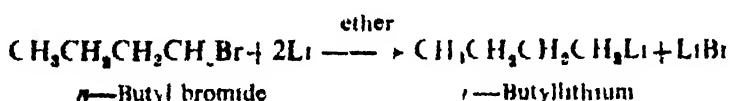


22.4 ORGANOLITHIUM COMPOUNDS

Organolithiums possess the general formula RLi . Because of the small size and high polarizing power of lithium, organolithium compounds have more ionic character than the Grignard reagents. They are readily soluble in paraffin solvents.

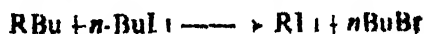
Preparation

1 Alkyl lithium derivatives can be prepared by the interaction between an alkyl halide and lithium metal in dry ether which provides a convenient medium in which organometallic compounds are usually soluble.



A solution of the organic halide in dry ether is added slowly to lithium wire. The mixture is stirred at -10°C . The resulting solution is used as it is for further work. Other organolithium compounds can be prepared by the same general method.

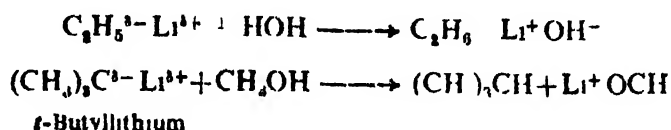
Organometallic that cannot be readily prepared directly from the metal and the halide can be obtained by *metal-halogen interconversion* as illustrated below.



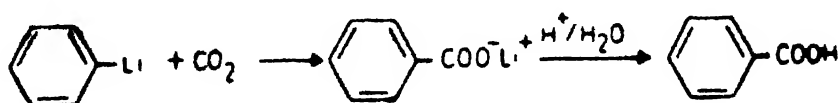
Reactions

Organolithiums are considerably stronger bases than the organomagnesium compounds and are thus employed in the initiation of many anionic rearrangements.

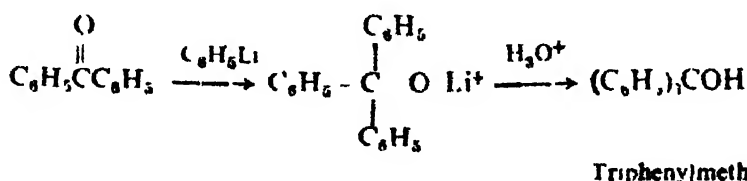
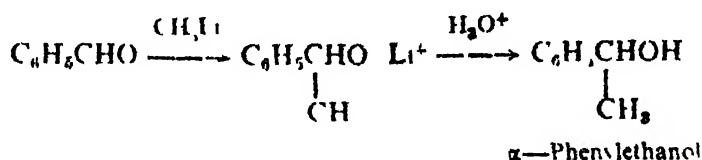
1. **Reaction with Water:** A hydrocarbon is evolved on treatment of an organolithium with water. It is thus essential to work with these reagents in the absence of moisture. These reactions are nothing but acid base reactions



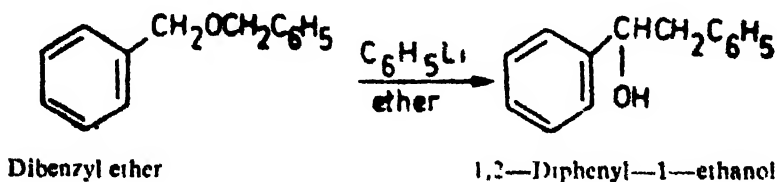
2. **Carbonation:** Like the Grignard reagents, carbonation of organolithium leads to carboxylic acid



3. **Reaction with Carbonyl Compounds:** Organolithium compounds are very reactive and powerful nucleophiles. They give better yields of alcohols from carbonyl compounds than the corresponding Grignard reagents

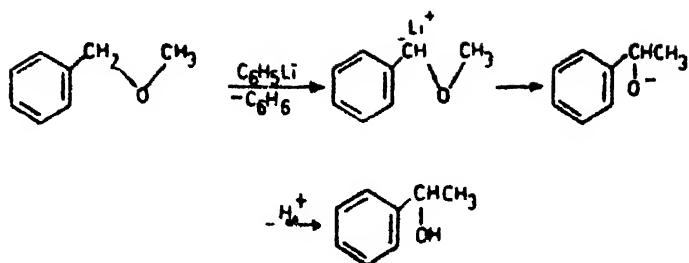


4. **Wittig Rearrangement:** In this reaction alkyl-benzyl and related ethers are converted to carbinols in the presence of phenyl- or alkyl lithium

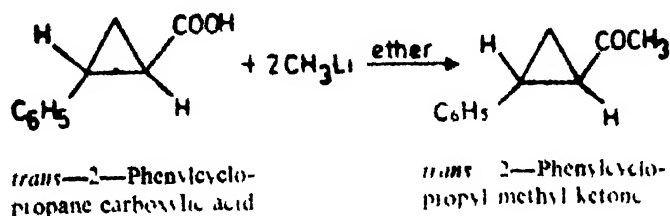


Mechanism

Phenyllithium abstracts a proton to form a carbanion which undergoes rearrangement. The intermediate on acidification forms a carbinol.



5. Under appropriate conditions carboxylic acids react with methyl-lithium to form methyl ketones in a better yield than the Grignard reagents.

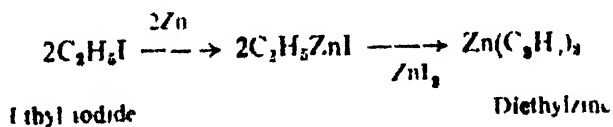


22.5 ORGANOZINC COMPOUNDS

Organozinc compounds are relatively unstable and are not much used in preparative organic chemistry.

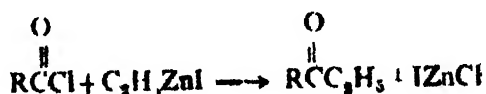
Preparation

1. Organozinc compounds, in general, may be obtained by heating an alkyl halide with zinc metal followed by distillation of the resultant alkyl-zinc halide.

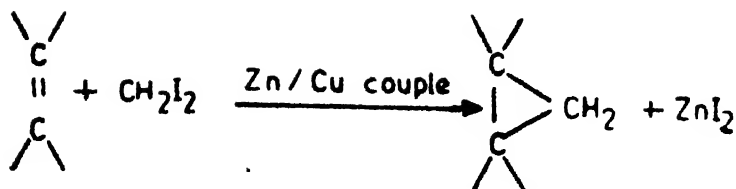


Reactions

1. In addition to organomagnesium compounds, they are used in the preparation of ketones from acid chlorides.



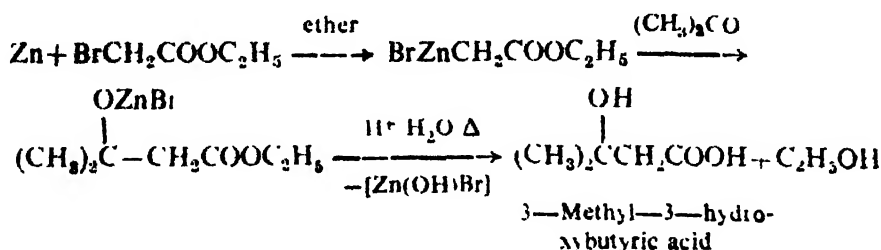
2. The attacking reagent in methylene insertion into the carbon-carbon double bond occurs through an organozinc compound.



An alkene

A cyclopropane

3. The Reformatsky Reaction : The Reformatsky reaction for the preparation of hydroxy acids also proceeds through the formation of an organozinc compound



A common side-reaction is the self-condensation of the α -halo ester during the zinc enolate ion formation, which after hydrolysis yields a β -keto ester. Organozinc reagents are preferred to lithium or magnesium reagents because the latter cannot be prepared from esters.

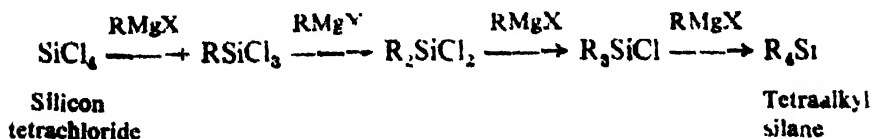
22.6 ORGANOSILICON COMPOUNDS

Silicon is a non-metallic element, though it has some metallic properties as well. It lies in the same group (IV) of the Periodic Table as carbon. Alkylsilanes behave similarly to saturated hydrocarbons but the former are thermally less stable. The alkylsilanes are generally colorless oils.

Preparation

Alkylsilanes are obtained by progressively replacing the hydrogen atom from the simplest silicon hydride, SiH_4 (b.p. -112°C) with alkyl groups.

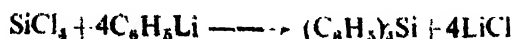
1. By the action of Grignard reagent on silicon tetrachloride



2. Dialkylzinc may be used in place of Grignard reagent in the preparation of organosilicon compounds.

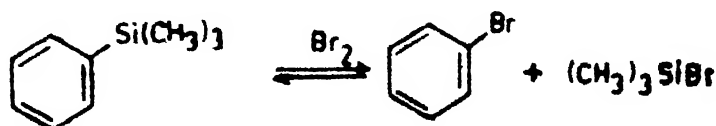


Alkylolithiums function similarly, and react with silicon halides.

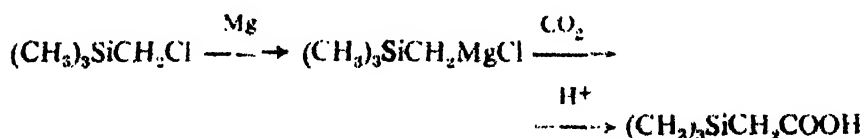


Reactions

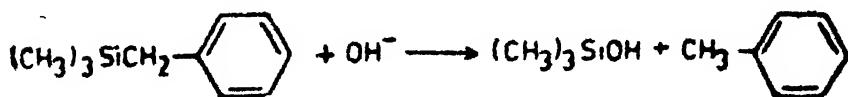
1. The silicon-carbon bond is easily cleaved by electrophilic reagents even without the aid of a catalyst.



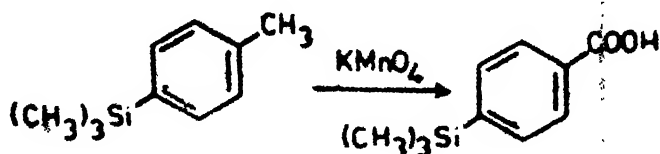
2. Alkyl chloro silanes form Grignard reagents with magnesium which on carbonation yield acids.



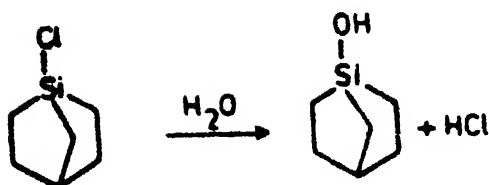
3. The silicon—carbon bond is also cleaved by nucleophiles.



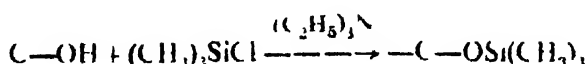
4. The silicon—carbon bond is resistant to oxidation, and is thus not affected by oxidizing agents.



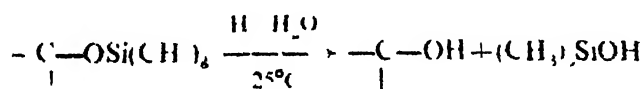
5. In marked contrast to carbon bridgehead halides, the silicon analogues react rapidly in nucleophilic displacement reactions.



6. Trimethylchlorosilane is employed for the protection of a primary alcoholic group



The silyl ether linkage is stable to most basic and neutral solutions but can be easily cleaved by mild aqueous acid



22.7 ORGANOBORANES

As was discussed in Chapter 1, boron is trivalent and forms predominantly covalent sp^2 hybridized bond with other elements, such as boron trifluoride BF_3 or trimethylborane $\text{B}(\text{CH}_3)_3$.

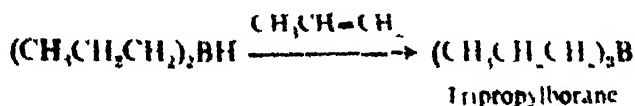
The simplest hydride of boron is BH_3 , which is not stable and exists in a dimeric form, known as diborane, B_2H_6 . Diborane is a gas and its solution in ether, THF or diglyme is employed for synthetic purposes. Higher hydrides are stable. Organoboranes are usually named as derivatives of borane.



Many boron-oxygen compounds derive their names from boric acid $\text{B}(\text{OH})_3$, boronic acid $\text{HB}(\text{OH})_2$, etc. for instance, phenyl boronic acid $\text{C}_6\text{H}_5\text{B}(\text{OH})_2$.

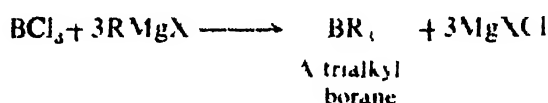
Preparation

1. A useful method of preparing trialkylboranes is by the addition of B_2H_6 to alkenes or alkynes.



This process is called *hydroboration*. The boron atom attaches to the carbon atom of the double bond having the larger number of hydrogens. In other words, addition follows the Markownikoff's rule, boron is more electropositive than hydrogen. Mechanistically the addition takes place in a stereospecific *cis*-manner i.e., both boron and hydrogen add from the same side of the double bond.

2. *From Halo- or Alkoxy boranes.* A trivalent borane is electrophilic in nature and is easily attacked by a carbanion generated from organometallic compounds of Mg, Li, Zn, etc.,



Mono- or dialkyl-boranes may be obtained by this method depending on the nature of X and R, and the temperature of the reaction.

Trialkylboranes are colorless liquids with an odor of onions. They are unstable to atmospheric oxygen. Triphenylborane is relatively stable.

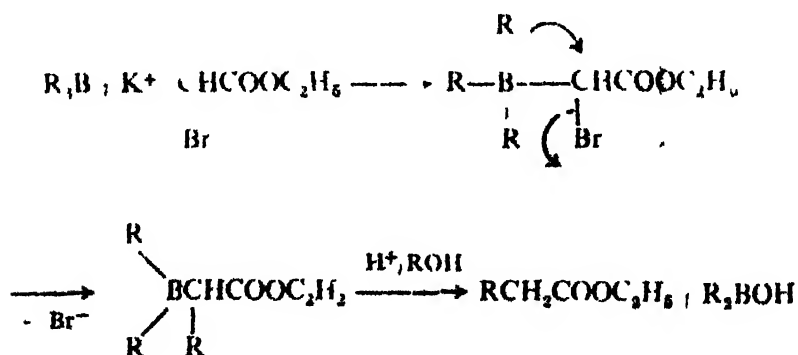
Reactions

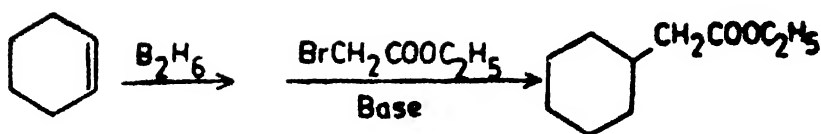
Organoboranes have emerged as highly versatile intermediates in organic syntheses. These reactions are quite different from those involving conventional organometallics such as the Grignard reagents. The carbon—boron bond is highly covalent and can be cleaved by a variety of reagents.

1. *Oxidation:* The boron-carbon bond in trialkylboranes is cleaved by oxygen to form mono- or dialkoxy-boranes.

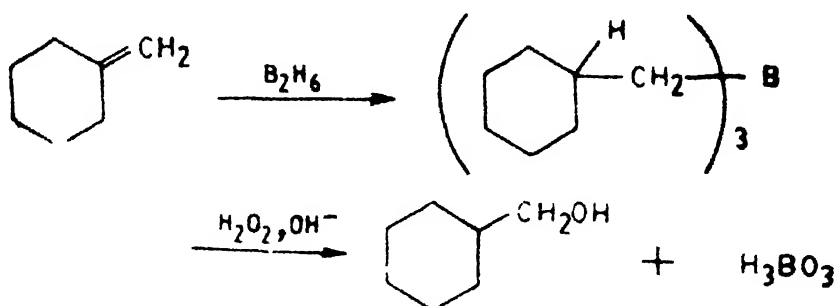


2. *Reaction with Enolate Ions.* Trialkylboranes undergo reaction with an enolate ion with its resultant alkylation.

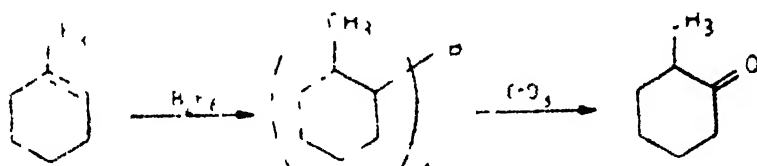




3. Organoboranes on oxidation with alkaline hydrogen peroxide yield alcohols



Oxidation of alkylboranes with a strong oxidizing agent provides a ketone

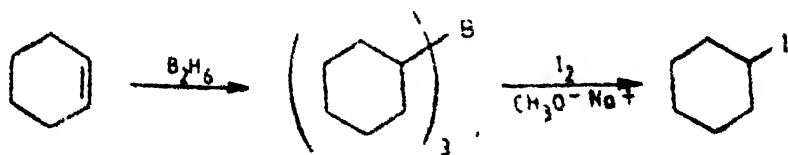


For the preparation of aldehydes and ketones see Chapter 17.

4. Alkylboranes undergo protonation with a carboxylic acid to yield a hydrocarbon. This provides a method for the reduction of carbon—carbon double bond

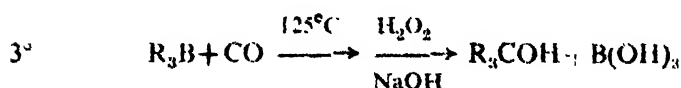
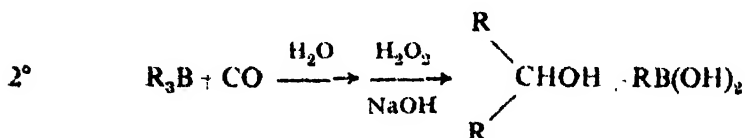
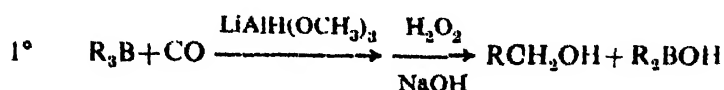


5. Alkylboranes offer a method of preparing alkyl halides. An alkylborane on treatment with iodine in the presence of a base ($\text{CH}_3\text{O}^- \text{Na}^+$ CH_3OH) yields an alkyl iodide



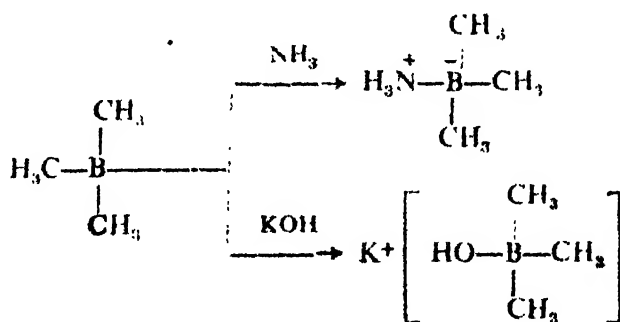
Alkyl bromides can be obtained similarly by treating with bromine.

6. *Preparation of Alcohols*: Carbonylation of trialkylboranes and subsequent reactions with different reagents yields alcohols



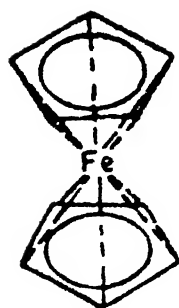
These reactions have complex mechanisms.

7. *Formation of Addition Compounds*: Because of the tendency of boron to accept a pair of electrons from such atoms as N, C, O, etc., trialkylboranes form addition compounds.



22.8 FERROCENES

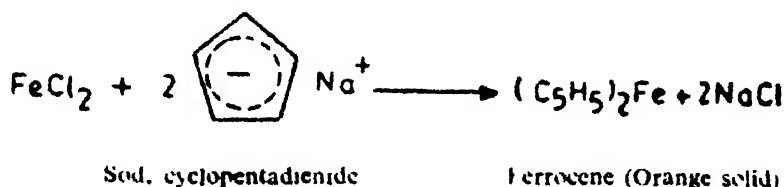
Ferrocenes are π -bonded organometallic complexes with the following structure. This class of compounds was discovered in 1952. The π -electrons of ferrocene are associated with both the 5 carbon atom rings and the iron atom. In ferrocene the carbon-iron bonding is a result of the overlap between the inner lobes of the p -orbitals of the cyclopentadienyl anions and the $3d$ orbitals of the iron atom. Since an iron atom is complexed between two flat cyclopentadiene rings, such compounds are also known as *organometallic sandwich compounds*. They display aromatic character. The C—C bond distances are all 1.40 Å and C—Fe bond distances are all 2.04 Å. Ferrocene



is an orange solid, m p 174°C . It contains 12π electrons and is a highly stable compound

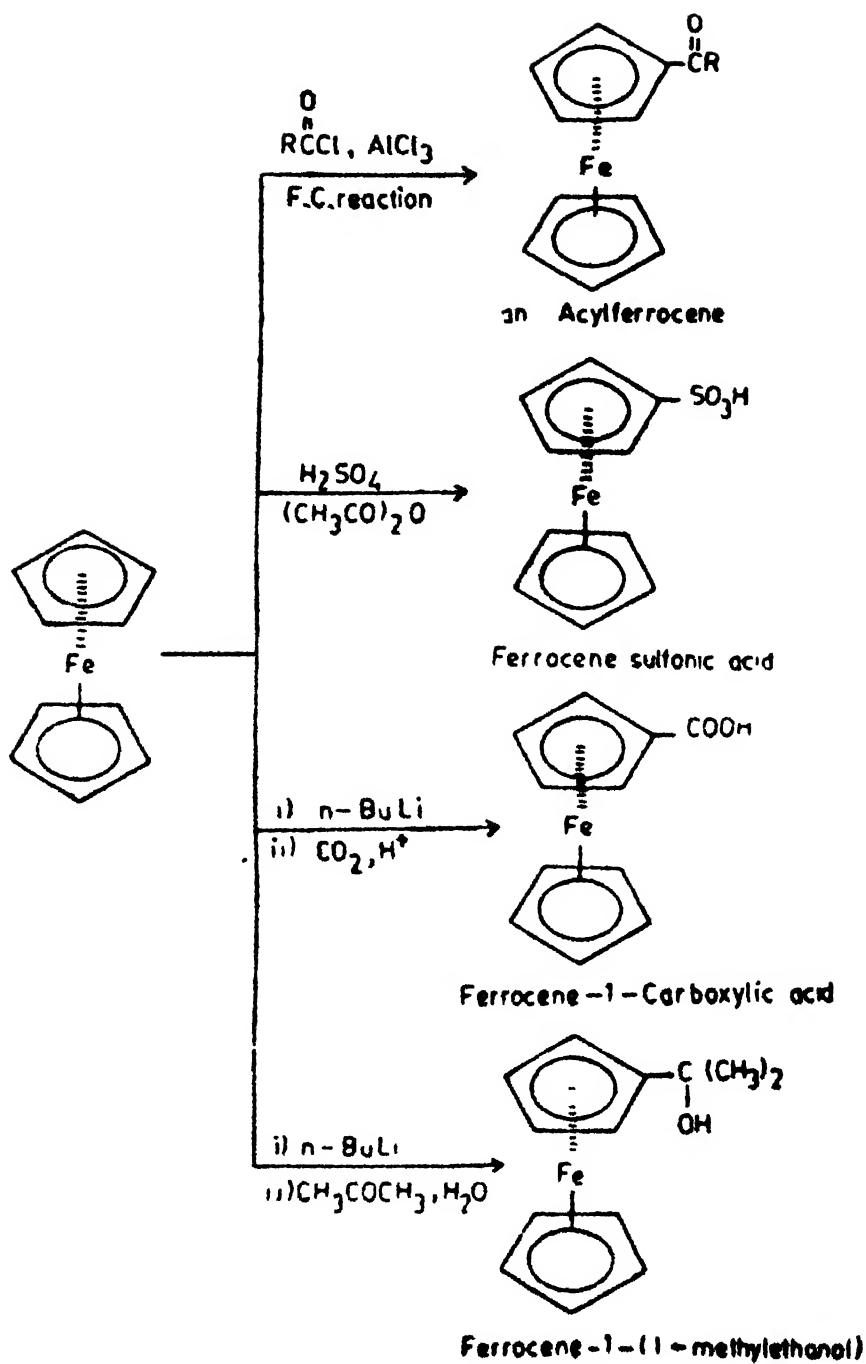
Preparation

1. The most convenient laboratory method for the preparation of ferrocenes is by reacting one equivalent of ferrous chloride with two equivalents of cyclopentadienyl anion



Reactions

Ferrocene shows aromatic behavior and undergoes a number of reactions similar to those exhibited by many aromatic hydrocarbons



The discovery of ferrocene was followed by the preparation of a number of similar organometallic compounds. These compounds, as a class are called *metallocenes*. Metallocenes with five to eight membered rings have been synthesized containing metals such as cobalt manganese nickel uranium, etc

QUESTIONS

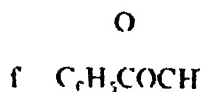
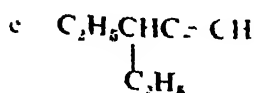
22 1 Methylmagnesium bromide is combined with each of the following compounds and then with water. What products are obtained in each case?

a HBr (dry)



c $\text{CH}_3\text{CH}_2\text{CN}$

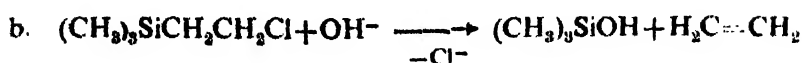
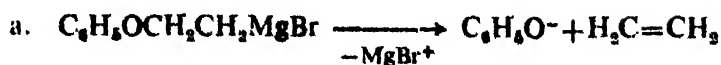
d H_2CO



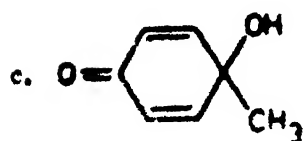
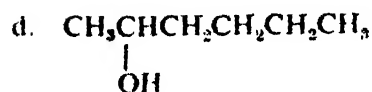
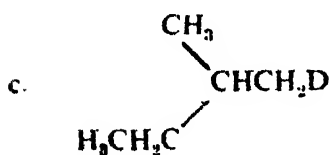
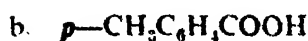
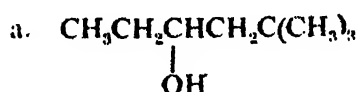
g $\text{C}_2\text{H}_5\text{OH}$

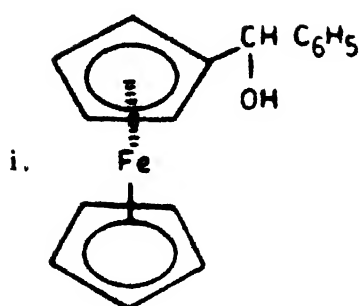


22.2 Suggest mechanisms for the following reactions:



22.3 Synthesize the following compounds starting from suitable reagents:





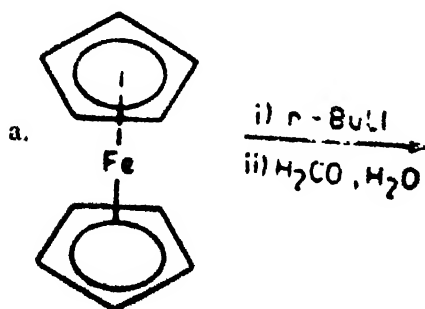
22.4 How will you show that ferrocene behaves like an aromatic compound?

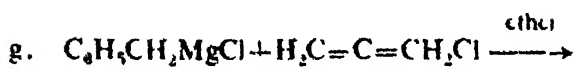
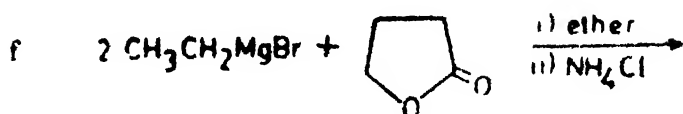
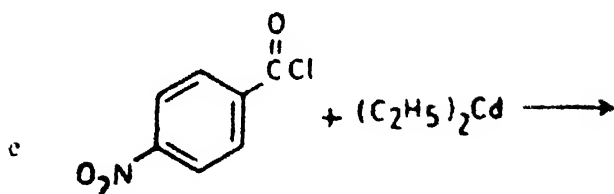
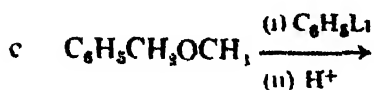
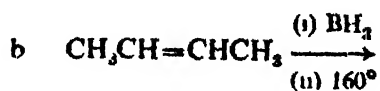
22.5 Prepare the alcohol $(\text{C}_6\text{H}_5\text{C}(\text{CH}_2\text{CH}_3)_2\text{OH})$ from three different starting materials using only Grignard reagents.

22.6 What are organometallic compounds? Describe the preparation and properties of organo-boranes

22.7 How would you prepare toluene—4—/ from benzene?

22.8 Write the products of the following reactions





- 22 9 a. Suggest a mechanism for the Reformatsky reaction
 b. Why cannot Li or Mg be used in place of Zn in the Reformatsky reaction?

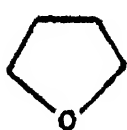
22 10 Give, in each case the reagent you would use to convert isopropyl magnesium bromide to the following compounds

- a $(\text{CH}_3)_2\text{CHI}$
 b $[(\text{CH}_3)_2\text{CH}]_3\text{P}$
 c $(\text{CH}_3)_2\text{CHCOOH}$
 d $(\text{CH}_3)_2\text{CHD}$
 e $(\text{CH}_3)_2\text{CHCH}=\text{CH}_2$
 f $(\text{CH}_3)_2\text{CHCH}_2\text{OH}$

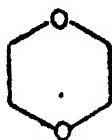
- 22.11 How can Grignard reagents be prepared? What special precautions are to be taken into consideration? How can it be used to prepare (a) propionic acid, (b) *n*-butyl alcohol, (c) trimethylcarbinol, (d) propionaldehyde.
- 22.12 An organic compound A, has the molecular formula C_2H_5Br . A solution of this compound in ether, on treatment with magnesium turnings gives a compound B. Treatment of compound B, with ethyl acetate followed by hydrolysis gives a compound C, containing no magnesium. The compound C is known to give an orange colored precipitate with 2,4—dinitrophenylhydrazine. Give possible structures for A, B and C. Explain the reactions involved above and also give the reaction of B with acetic acid.
- 22.13 What is a Grignard reagent? How will you bring about the following changes with its help? (a) ethyl bromide to propane (b) ethyl iodide to propionic acid (c) acetylene to 1—butene (d) acetaldehyde to acetone (e) ethanol to isopropyl alcohol.
- 22.14 (a) How is ethylmagnesium bromide prepared in the laboratory? What important precautions are to be taken for its preparation? (b) How can it be converted into (i) propionic acid, (ii) *n*—butyl alcohol, (iii) propionaldehyde, (iv) ethyldimethylcarbinol.
- 22.15 Offer explanation for the following :
- Why should Grignard reagent be prepared with the exclusion of moisture?
 - Can an ester be used to prepare a ketone via the Grignard reaction?
 - Does ferrocene display aromatic behavior? Explain.

Heterocyclic Compounds

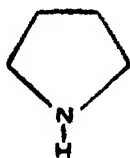
A cyclic organic compound containing all carbon atoms in ring formation is referred to as *carbocyclic compound*. If at least one atom other than carbon forms a part of the ring system then it is designated as a *heterocyclic compound*. Heterocyclic compounds containing nitrogen, oxygen and sulfur are by far the most common. The chemistry of heterocyclics offers an interesting class of organic compounds. Many important natural products such as alkaloids, chlorophyll, vitamins, drugs, etc., are derivatives of simple five- or six-membered nitrogen heterocycles. Depending on their structures, heterocyclic compounds are classified as non-aromatic and aromatic. Examples of some non-aromatic compounds are given below :



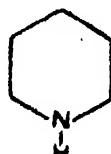
Tetrahydrofuran



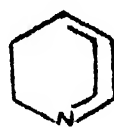
1,4-Dioxane



Pyrrolidine



Piperidine



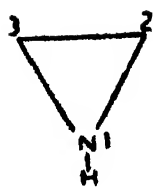
Quinuclidine

They possess physical properties typical of the particular hetero atom present in the ring. For instance, THF and dioxane have properties characteristic of an ether, piperidine behaves like a secondary amine while quinuclidine behaves like a tertiary amine.

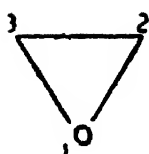
The aromatic heterocyclic compounds possess considerable resonance energies and have some properties which typify the chemistry of benzene. The hetero atom can play an extremely important part in determining the properties of compounds of this type. In addition, there are a number of cyclic compounds which are, strictly speaking, heterocyclic, such as acid anhydrides, lactones, acetals and ketals, but are not considered as such.

23.1 NOMENCLATURE OF HETEROCYCLIC COMPOUNDS

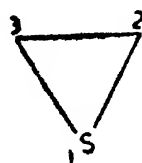
In heterocycles, since one of the atoms is different than carbon, this atom is assigned position-1. Representative examples of some heterocyclic compounds are given below:



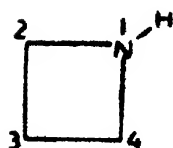
Aziridine



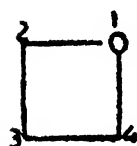
Oxirane



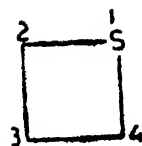
Thirane



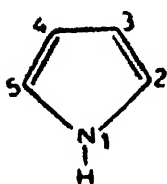
Azetidine



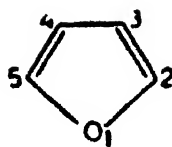
Oxetane



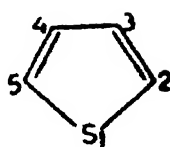
Thetane



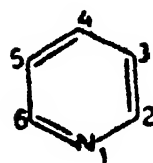
Pyrrole



Furan

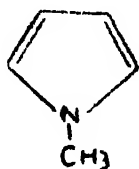


Thiophene

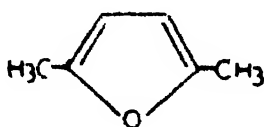


Pyridine

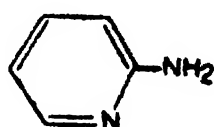
Substituents located on the ring are given the lowest number by moving around the ring. Besides, Greek alphabet letters are also used to specify the position of the substituents. The methyl- and carboxyl-derivatives of pyri-



1—Methylpyrrole

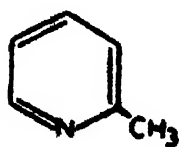
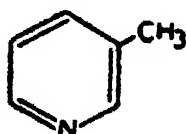
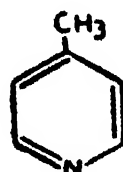


2,5—Dimethylfuran

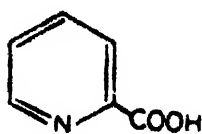


2—Aminopyridine

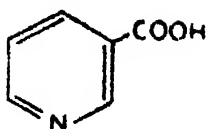
dine also possess the special names of *picolines*.

2—Methylpyridine
(α —Picoline)3—Methylpyridine
(β —Picoline)4—Methylpyridine
(γ —Picoline)

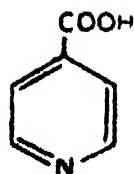
The dimethyl derivatives are called *lutidines*



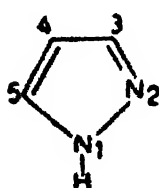
Pyridine-2-carboxylic acid
(Picolinic acid)



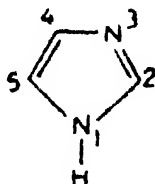
Pyridine-3-carboxylic acid
(Nicotinic acid)



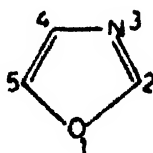
Pyridine-4-carboxylic acid
(iso Nicotinic acid)



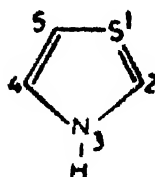
Pyrrole



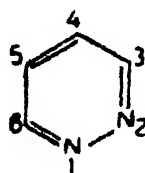
Imidazole



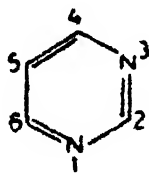
Oxazole



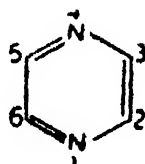
Thiazole



Pyridazine

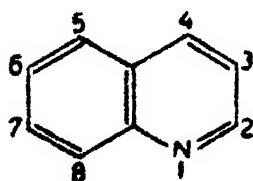


Pyrimidine

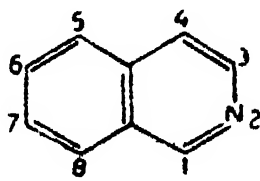


Purine

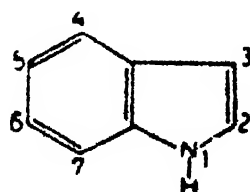
The numbering in condensed ring systems also commences at the hetero atom as shown in the following compounds



Quinoline



Iso-Quinoline



Indole

23.2 FIVE-MEMBERED RING SYSTEMS

The simple five-membered heterocyclic ring systems are pyrrole, furan and thiophene. Each of these contains two double bonds in the ring and one may anticipate that these would behave like dienes. But this is not so, they display typical properties of an aromatic ring. For instance, they undergo substitution rather than addition and possess high resonance energies—pyrrole (21.0 kcal/mole), furan (18.5 kcal/mole), and thiophene (27.7 kcal/mole). The resonance energies decrease in the order thiophene > pyrrole

> furan. However, certain derivatives of furan and pyrrole participate in Diels—Alder reactions while no D—A adduct is known to form with thiophene under normal conditions. Their aromatic character is further recognized from the delocalization of electrons on the hetero atom into the ring, and a comparison of dipole moments measured for these compounds and their tetrahydro derivatives.

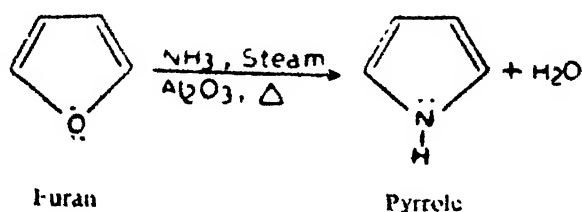
All these compounds undergo electrophilic aromatic substitution which is characteristic of aromatic compounds and are even more reactive than benzene.

23.2.1 Pyrroles

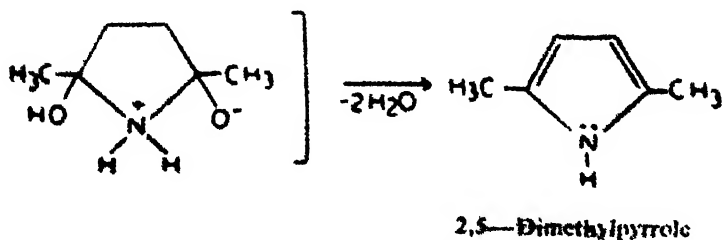
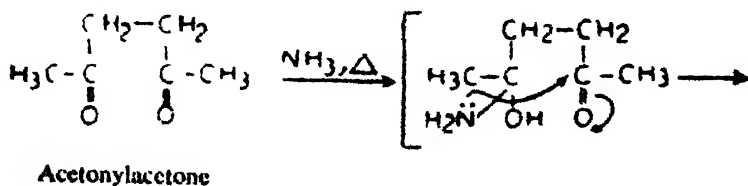
Pyrrole is found in coal tar and in chlorophyll of plants. Its vapors cause the red coloration of a pine splint moistened with hydrochloric acid.

Preparation

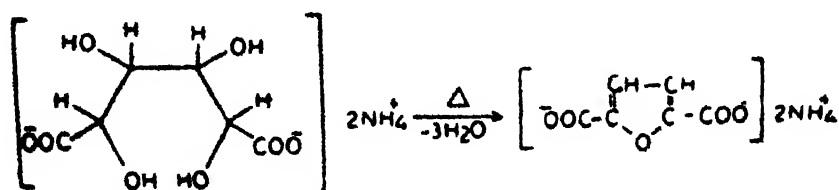
1. Commercially, pyrrole is obtained by passing a mixture of furan, ammonia and steam over heated aluminum oxide as catalyst.



2. *The Paul—Knorr Synthesis:* This method involves the heating of an enolizable 1,4—diketone with ammonia or a primary amine. Pyrrole itself is formed from succinaldehyde and ammonia while 2,5—dimethylpyrrole is obtained from acetylacetone and ammonia.

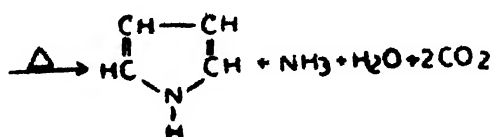


3 Heating ammonium mucate with glycerol at 200° yields pyrrole in about 45% yield, and is a classical method for its preparation in the laboratory



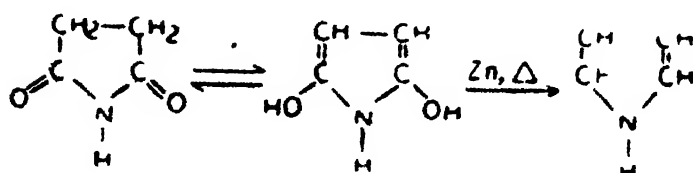
Ammonium mucate

Ammonium dehydromucate



Pyrrole

4. Distillation of succinimide in the presence of zinc dust results in pyrrole formation

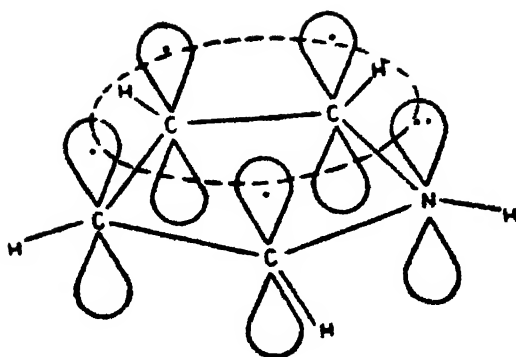


(Diketo-form)

(Dienol form)

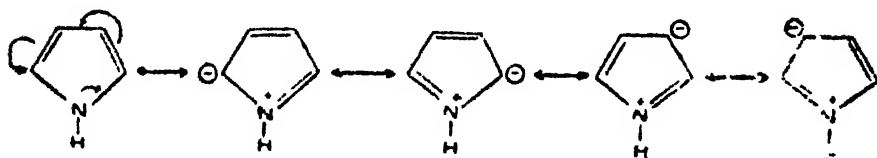
Properties

Pyrrole is a colorless liquid, b.p. 131°, but turns brown gradually in air. It is sparingly soluble in water but is readily miscible with ether and alcohol. It behaves like an aromatic compound with a resonance energy of 21 kcal/mole. From its structure, it appears to be a secondary amine but it is only very weakly basic. The reason for this low basicity is that the lone pair on the nitrogen atom participates in resonance with the π bonds of the ring in the same manner as in benzene. The electrons are thus not available for bonding with a proton. Pyrrole is thus virtually non-basic, $\text{P}K_b$ 13.60. The delocalization of the electrons is further confirmed by a relatively high value of the dipole moment which points away from the nitrogen atom.

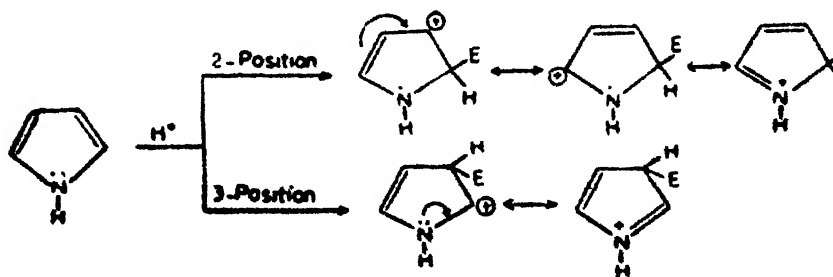


Orbital Representation of Pyrrole

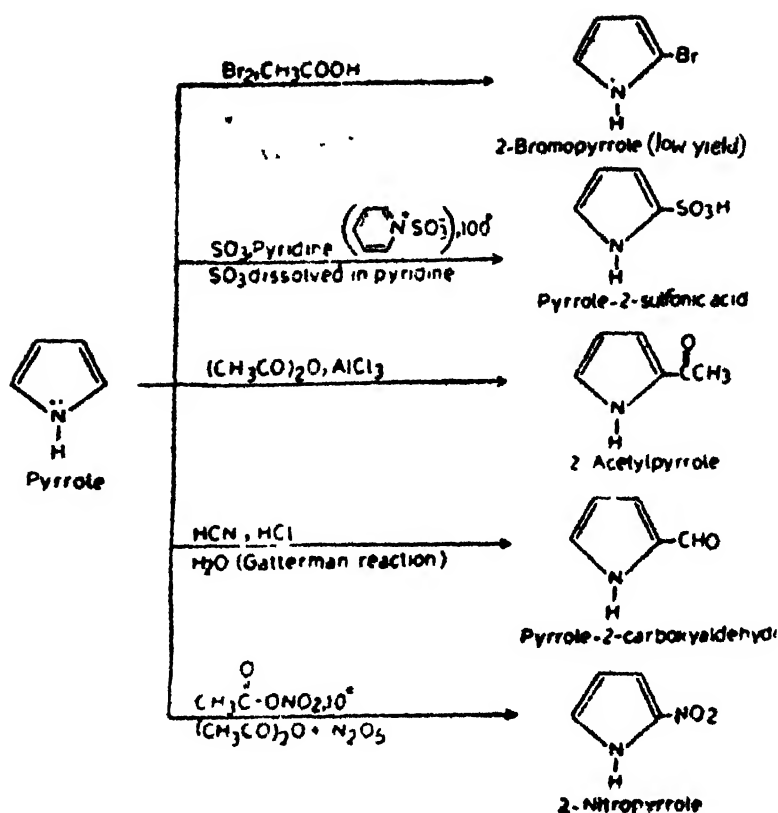
The following resonance structures of pyrrole are important.



1. *Electrophilic Substitution:* This is one of the most important reactions of heterocyclic compounds. In pyrrole, the attack of an electrophile takes place at the 2- and 5-positions because of the proximity of these positions to the nitrogen atom. The orientation can be rationalized by considering the resonance structures of the intermediate ions.

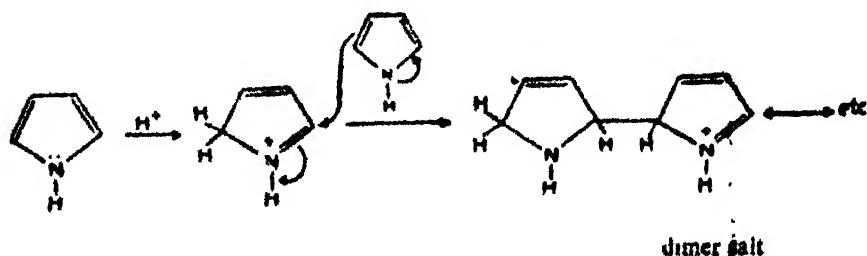


The charge is more delocalized when the attack takes place at 2-position than at 3-position. Pyrrole is much more reactive than benzene because of the delocalization of the nitrogen electron pair into the ring. Chlorination of all the five-membered heterocycles affords a mixture of products. Also alkylation under the Friedel—Crafts condition has not been very successful.



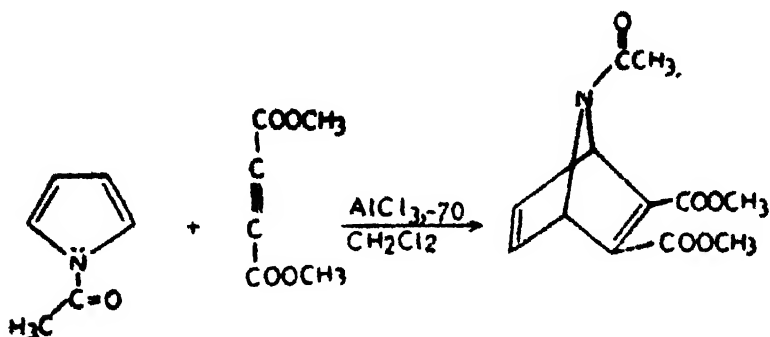
Pyrrole with chlorine yields a tetrachloro derivative.

2. *Salt Formation:* Pyrrole is a very weak amine; salt formation occurs at the expense of its aromatic character. The protonation takes place at the carbon atom. The diene-like intermediate polymerizes readily.

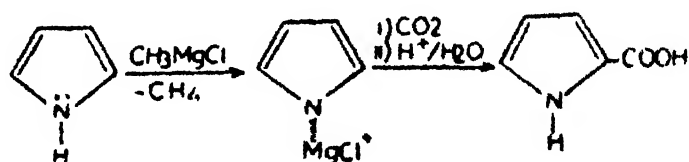


3. *Reaction with Dichlorocarbene:* Dichlorocarbene adds to a molecule of pyrrole to give 3-chloropyridine, a product of ring expansion and pyrrole 2-carboxyaldehyde via the Reimer-Tiemann reaction.

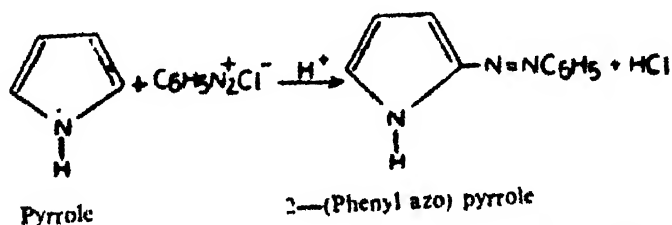
D—A adducts in the presence of aluminum chloride. The presence of electron-withdrawing groups on the nitrogen atom reduces the aromaticity of pyrrole. Therefore, N-acetylpyrrole forms a normal adduct with dimethylacetylene dicarboxylate (DMAD).



6 *Reaction with Grignard Reagents:* With a Grignard reagent and pyrrole, a salt is formed, which on carbonation and hydrolysis yields 2-carboxylpyrrole

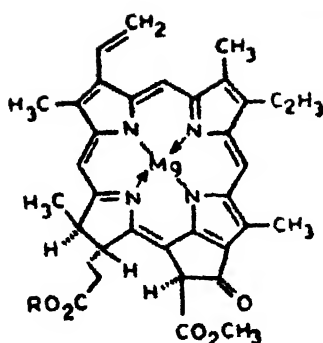


7. *Diazo Coupling:* Pyrrole couples with benzenediazonium chloride in an acid medium. This reaction shows that pyrrole is phenol-like character



Amongst the heterocyclic five membered rings, certain naturally occurring pyrrole derivatives are of particular interest.

The Porphyrins: Members of this biologically important group of natural products are the red pigment of blood, green coloring matter of leaves and vitamin B_{12} . Haemoglobin, is the pigment of the red-blood corpuscles. The green plant pigment is the magnesium complex of chlorophyll which occurs in the chloroplasts of plant cells. Vitamin B_{12} , the antipernicious factor, is closely related to the natural porphyrins. All these molecules contain pyrrole ring systems and possess complex structures. For instance, chlorophyll—a has the following structure:

(Chlorophyll—*a*)

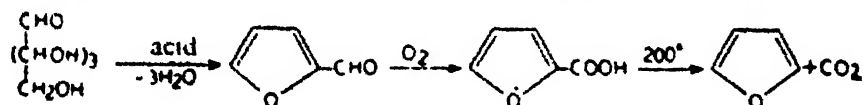
Chlorophyll—*a* is responsible for photosynthesis in plants

23.2.2 Furans

This ring system occurs in furanoses. It is obtained from the decomposition of sugars. The radical C_4H_5O is called *furyl*. Many furans give a characteristic green color with a pine splinter moistened with hydrochloric acid.

Preparation

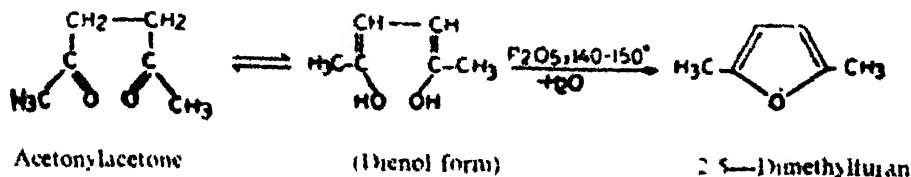
1. Furan is available chiefly from furfural which is obtained by the acid hydrolysis of polysaccharides in oat hulls or other naturally occurring substances such as corn cobs and starch which contain pentose fragments.



Pentose

Furan

2. *The Paul-Knorr Synthesis:* An enolizable 1,4—dicarbonyl compound on heating with a dehydrating agent such as phosphorus pentoxide or zinc chloride yields 2,5—dimethylfuran.



Acetylacetone

(Enol form)

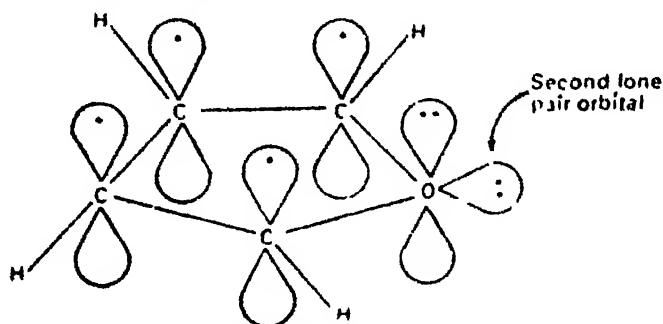
2,5—Dimethylfuran

Properties

Furan is a liquid, b.p. 32° and is soluble in most organic solvents. It is stable to air and alkali. In the presence of acid, it polymerizes to form insoluble, dark colored resins. Important resonance structures of furan are the following

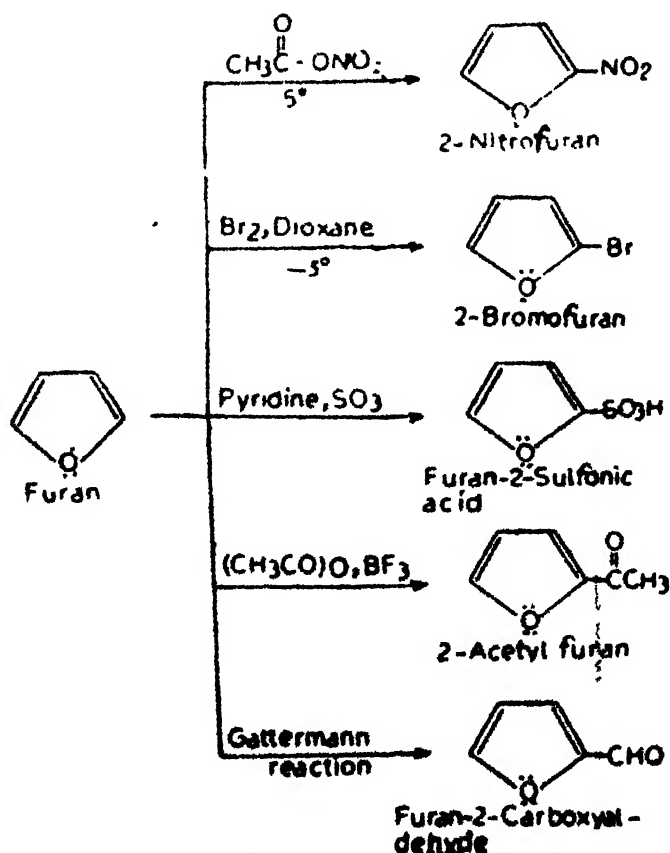


Furan and thiophene have similar structures. One electron pair of the oxygen atom is involved in aromatic sextet formation. The second lone-pair on the hetero atom occupies an sp^2 orbital that is perpendicular to the π -system of the ring, as shown below:



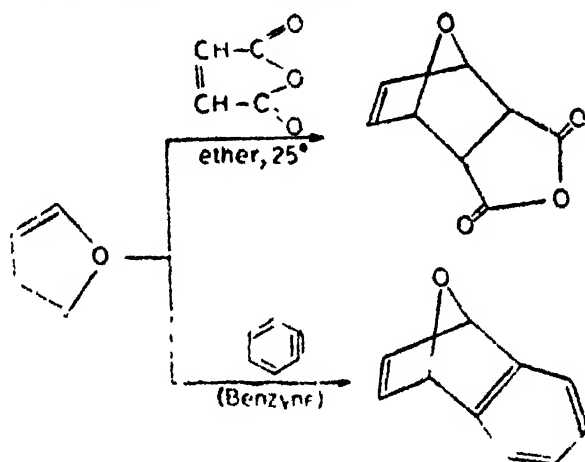
Orbital representation of furan

1. *Electrophilic Aromatic Substitution:* Analogous to pyrrole, furan also undergoes electrophilic substitution at the 2-position. The furan ring is labile to the action of acids

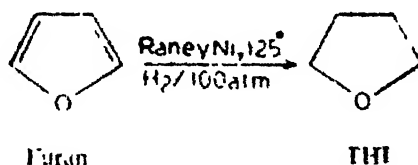


Treatment of furan with 1.6 moles of chlorine affords 2-chlorofuran in 64% yield.

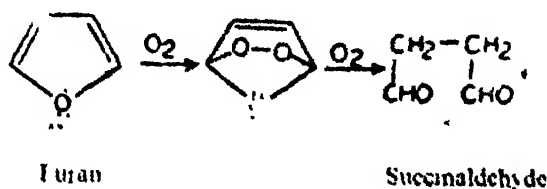
2. *The Diels—Alder Reaction:* Furan unlike pyrrole and thiophene, possesses diene properties and enters into Diels-Alder reaction with powerful dienophiles such as maleic anhydride and benzyne. No reaction occurs, however, with slightly less reactive dienophiles such as acrolein



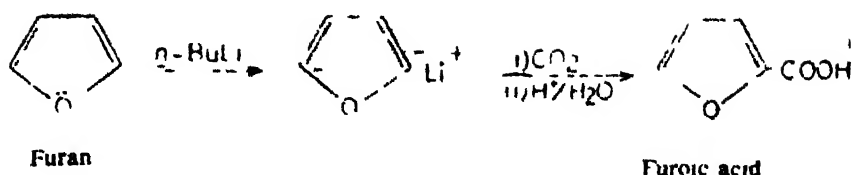
3. *Hydrogenation.* The furan ring is completely reduced in the presence of Raney nickel/hydrogen, yielding tetrahydrofuran (THF)



4. *Oxidation:* Furan is susceptible to oxidation and is unstable in the presence of air or oxygen and forms succinaldehyde. For storing furan it is stabilized by the addition of small quantities of hydroquinone. Air oxidation of furan results in a 2,5—addition product, i.e., a bridged peroxy adduct. This on further oxidation gives succinaldehyde.

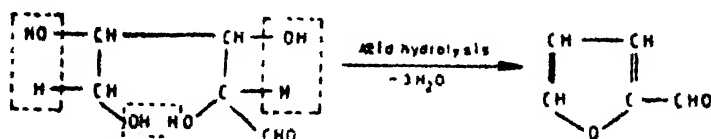


5. *Carbonation:* Furoic acid may be obtained as follows: A strong base effects deprotonation at the α -position of furan, the metallated furan on reaction with CO₂ and subsequent hydrolysis yields the acid.



23.2.3 Furfural

Furfural is formed by the action of dilute mineral acids on pentoses.

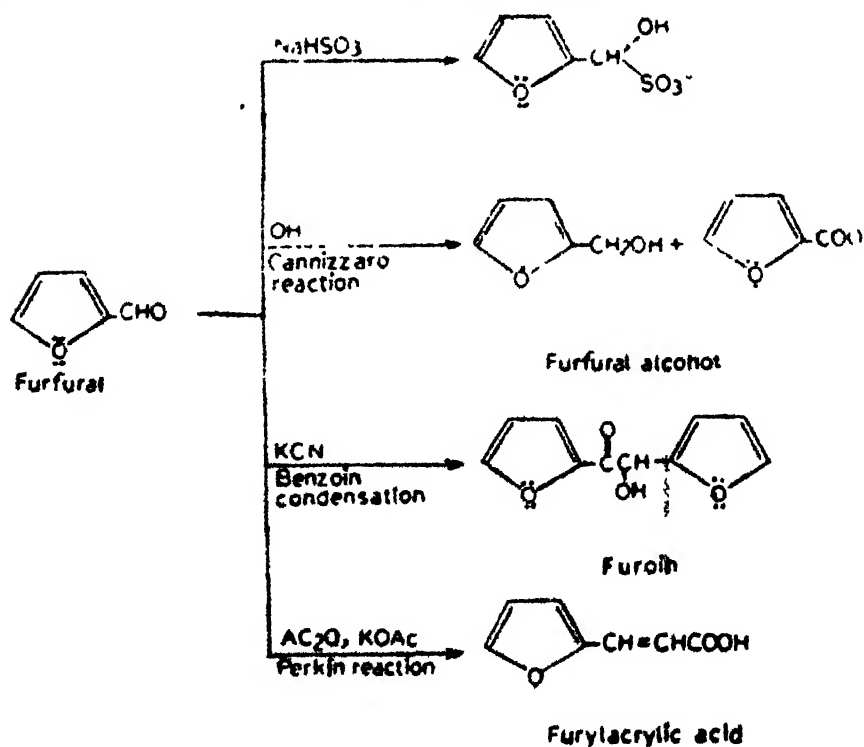


Furfural is available commercially and acts as a key starting material for many furan synthesis.

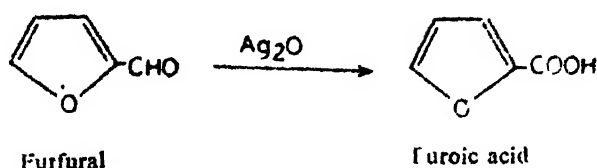
Properties

Furfural is a colorless liquid, b.p. 162° ; it rapidly turns brown in air. It is oxidized by bromine water to fumaric acid.

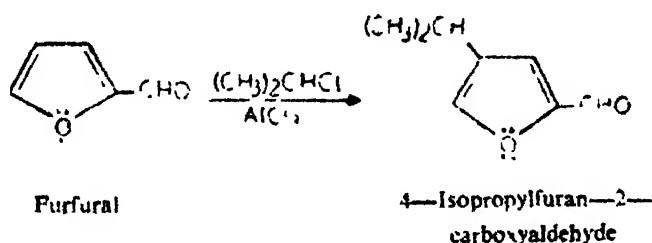
1. Furfural resembles benzaldehyde in its chemical behavior, and gives many reactions typical of an aromatic aldehyde.



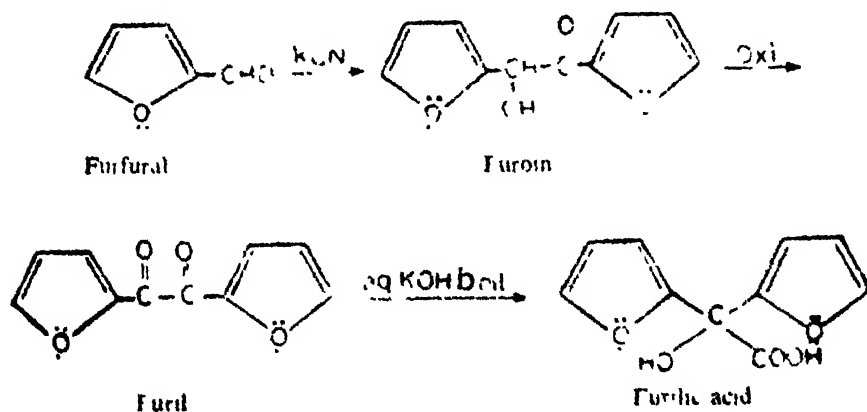
2. Furfural undergoes oxidation with a mild oxidizing agent like Ag_2O to furoic acid.



3. *Electrophillic Aromatic Substitution*: An electrophile attacks the ring at the 4-position in furfural, the reaction is faster than in the case of benzaldehyde.



4. Furfural yields furilic acid on treatment with base via the benzilic acid rearrangement



Uses

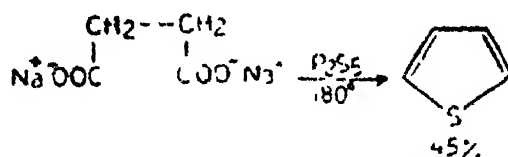
Furfural is used in the preparation of synthetic resins of the phenol-formaldehyde type and also as a selective solvent in petroleum refining.

23.2.4 Thiophenes

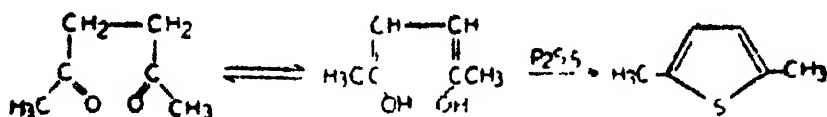
It is the sulfur analog of furan and occurs in coal tar and crude petroleum. The thiophene ring occurs in the vitamin B_1 (Thiamine) molecule.

Preparation

1 Thiophene may be obtained in the laboratory by the distillation of sod succinate with phosphorus pentasulfide, P_2S_5



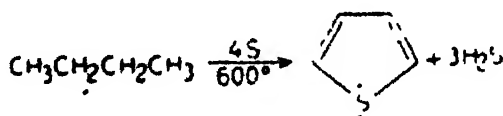
2. **The Paul—Knorr Synthesis:** As in the case of other five membered ring systems an enolizable 1, 4—diketone is heated with phosphorus pentasulfide to give thiophene.



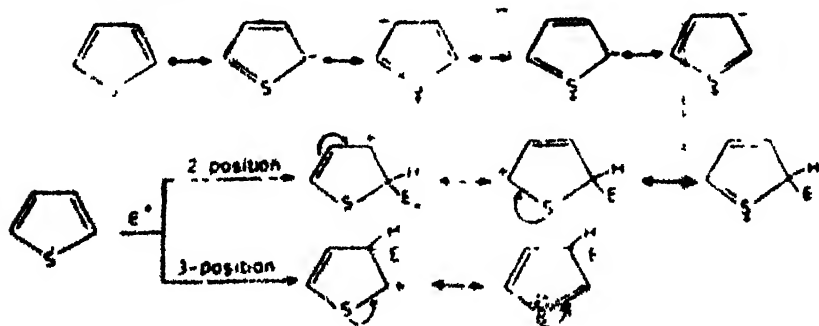
Acetylacetone

2,5—Dimethylthiophene

3. Commercially, thiophene is obtained from butane and sulfur in the vapor phase at 600° . The reactants are preheated to around 600° and then rapidly passed through a reaction tube and the exit gases containing thiophene are rapidly cooled.

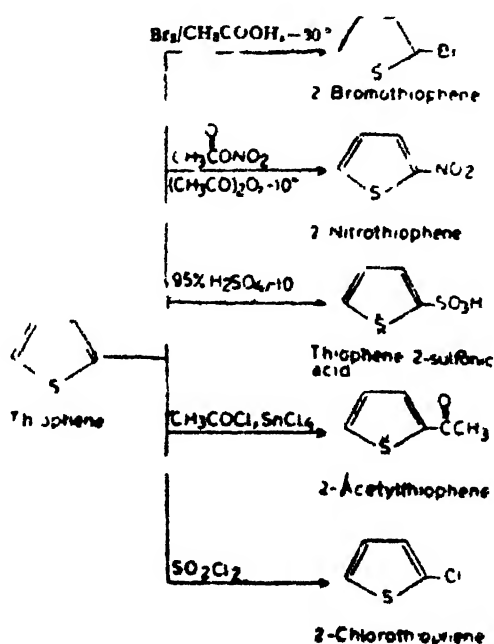
**Properties**

Thiophene is a colorless liquid, b.p. 80° (benzene b.p. 84°). It is miscible with water. Compared to pyrrole and furan it possesses a relatively high resonance energy of 28.7 kcal/mole. This order is also in agreement with the fact that sulfur atom is less electronegative than nitrogen and oxygen and releases electrons to a greater extent into the ring. Thiophene possesses the following important resonance structures

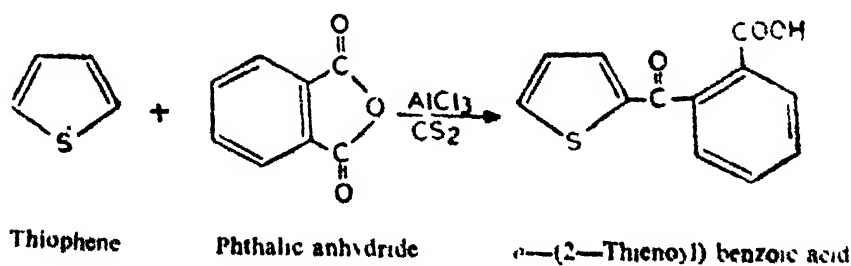


1. *Electrophillic Aromatic Substitution.* Thiophene is more easily substituted than benzene and the electrophile usually enters the 2-position as in pyrrole.

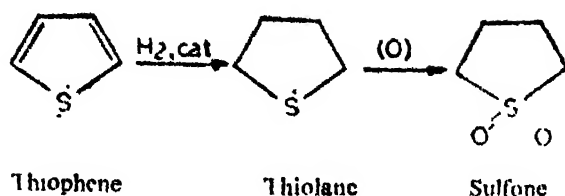
Thiophene is more stable towards acids than is furan. The 2-bromo devivative is also obtained on bromination with NBS in excellent yield.



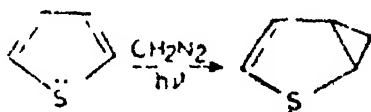
With phthalic anhydride and AlCl_3 in carbon disulfide, the Friedel—Crafts product is formed.



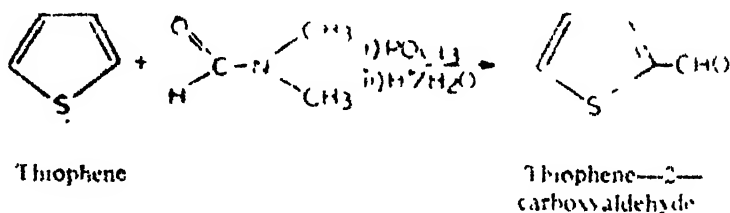
2. *Reduction:* On catalytic hydrogenation thiophene affords thiolane which on oxidation produces sulfone.



3. Thiophene undergoes a normal addition with a carbene at the C—C bond.

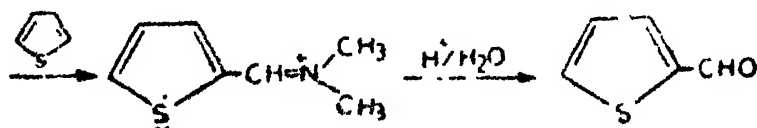
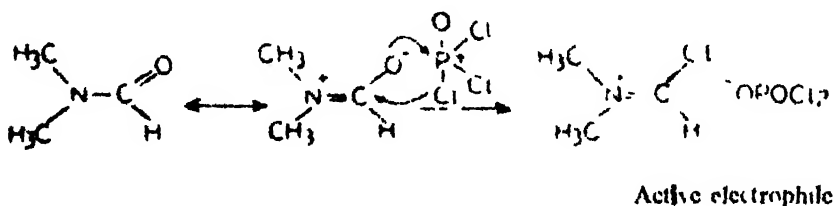


4. Thiophene—2—carboxyaldehyde results from the reaction of thiophene and dimethyl formamide in the presence of a Lewis acid (POCl_3).

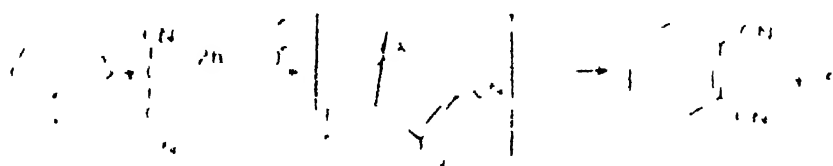


Mechanism

Dimethyl formamide reacts with POCl_3 in its dipolar form and yields the active electrophile. This attacks at 2—position of thiophene and hydrolysis of the resultant intermediate yields the aldehyde.



5. *The Diels—Alder Reaction:* Thiophene refuses to undergo the Diels—Alder reaction. The intermediate adduct if formed breaks down with the extrusion of sulfur



Thiophene

1,2-Dicyanobenzene

However, it has now been shown that thiophenes undergo the D—A reaction at high temperature and pressure

23.3 SIX-MEMBERED RING SYSTEMS

Amongst the six-membered heterocyclic compounds, we will discuss only pyridine

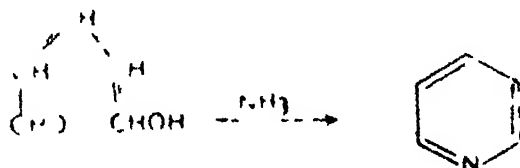
23.3.1 Pyridines

Pyridine is the simplest and probably the best known heterocyclic compound. It is an analog of benzene in which one of the methine (CH) group is replaced by a nitrogen atom. This change does not affect the aromatic character of the ring. Pyridine is found in coal tar and bone oil. Pyridine and piperidine are widely spread in natural products. Alkaloid nicotine contains the pyridine ring.

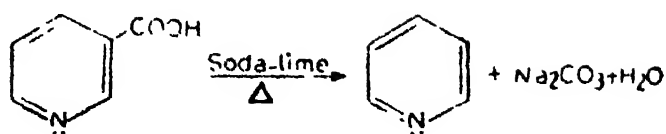
Preparation

1. Commercially pyridine is recovered from the light oil fraction obtained during the fractional distillation of coal tar. This fraction is treated with dil. sulphuric acid to dissolve pyridine as its salt. The aqueous layer is separated and neutralized with Na_2CO_3 and pyridine is regenerated as a dark brown oil. It is purified by fractional distillation (b.p. 115°).

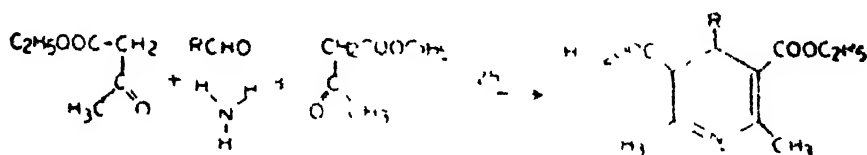
2. Pyridine is also obtained from the reaction of glucatonic aldehyde and ammonia. This method, however, has no practical value, as the yield is very poor.



3. A laboratory preparation of pyridine includes the distillation of nicotinic acid with soda—lime ($\text{CaO} + \text{NaOH}$)

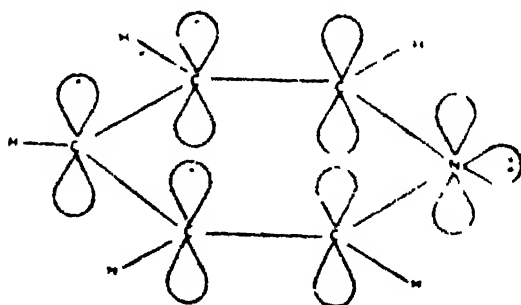


4. **The Hantzsch Synthesis:** This involves the condensation of a β -ketone ester with an aldehyde in the presence of ammonia.



Properties

Pyridine is a colorless liquid and is miscible with water in all proportions. It resembles benzene in terms of structure and overall stability. Like benzene it is extremely resistant to oxidizing agents. It possesses a resonance energy of 33 kcal/mole. The lone pair on the nitrogen atom is located in an sp^3 hybridized orbital which is perpendicular to the π -system of the ring. The

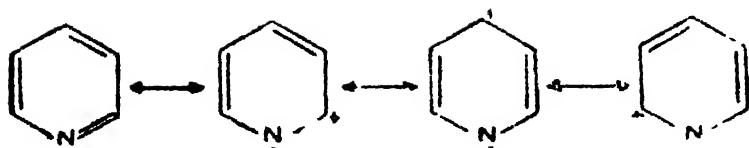


Orbital representation of pyridine

electron pair is, therefore, available for additional bonding. Pyridine is thus weakly basic ($\text{p}K_b = 5.2$) because involving a nitrogen or oxygen in multiple bonding makes the atom less basic, for instance,

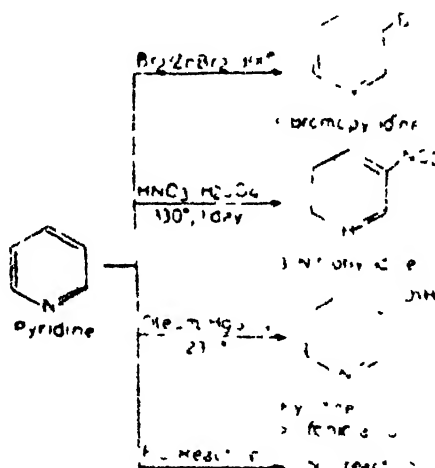
Pyridine	$K_b = 1.4 \times 10^{-6}$
Methylamine	$K_b = 4.38 \times 10^{-4}$

The resonance in pyridine molecule takes place as follows:

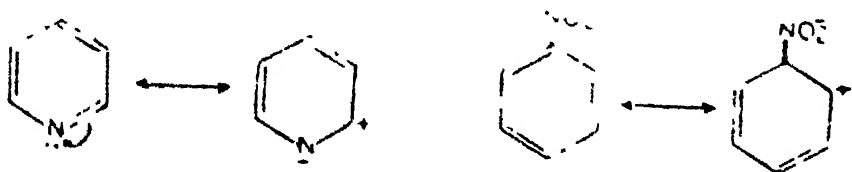


This is confirmed by its dipole moment which is equal to 2.26 D and points toward the nitrogen atom.

1 **Electrophilic Aromatic Substitution:** Because of the above resonance structures which makes the ring electron deficient it is apparent that an electrophilic attack on pyridine will take place only under drastic conditions, in contrast to benzene, in which this reaction takes place rather readily. Furthermore, under acidic conditions of such reaction the nitrogen atom of pyridine is protonated or complexed with a Lewis acid which further reduces its reactivity

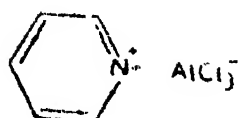


In an acid medium, the protonation of pyridine nitrogen atom imparts a high degree of positive character to the α - and γ -positions. In this regard it resembles nitrobenzene. The α - and γ -positions bear a formal resemblance to the o - and p -positions of nitrobenzene.

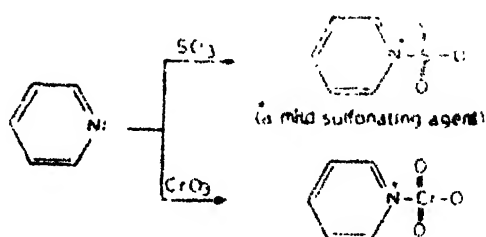


Similar to nitrobenzene, pyridine also does not undergo the $F.C.$ reaction because $AlCl_3$ itself forms an addition compound with pyridine of the type

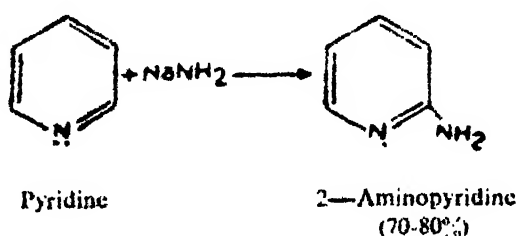
Shown below:



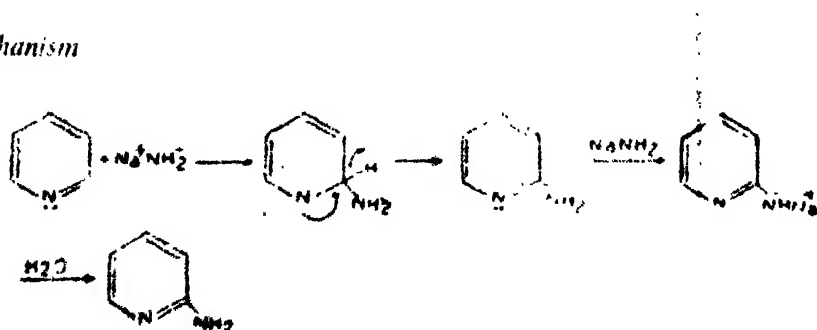
Other Lewis acids such as SO_3 and CrO_3 also form addition compounds with pyridine.



2. *Nucleophilic Substitution:* In contrast to benzene, a nucleophilic attack on the pyridine ring takes place with relative ease because of the dipolar structures. The attack takes place at the 2— and 4—positions. Direct amination of pyridine occurs on heating sodamide in dry toluene at 110° . This is referred to as the *Chichibabin reaction*.

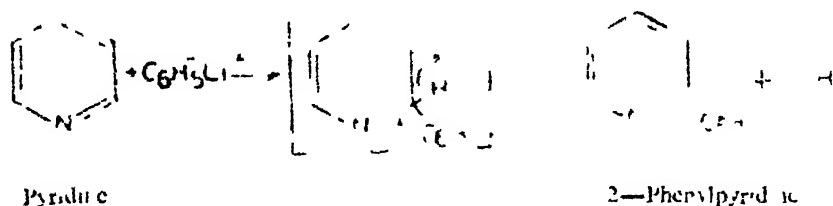


Mechanism

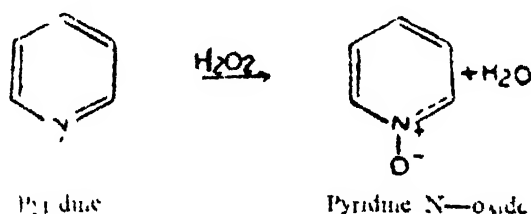


The amide ion attacks the 2—position and subsequent electron shift and ejection of hydride ion forms 2-aminopyridine.

b. An analogous nucleophilic substitution occurs on treating pyridine with phenyllithium, this enables the introduction of a phenyl group at the 2—position.

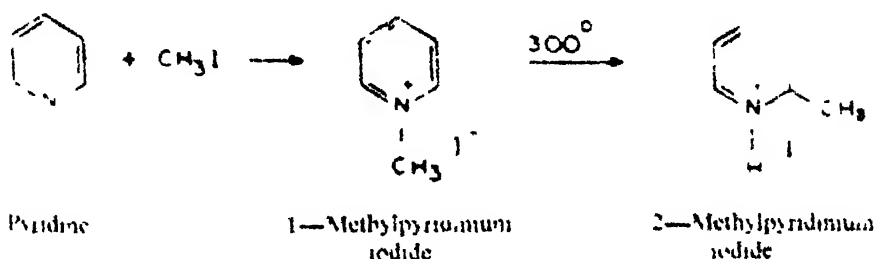


c. *Oxidation:* Pyridine is easily oxidized with H_2O_2 or perbenzoic acid to give pyridine N—oxide.



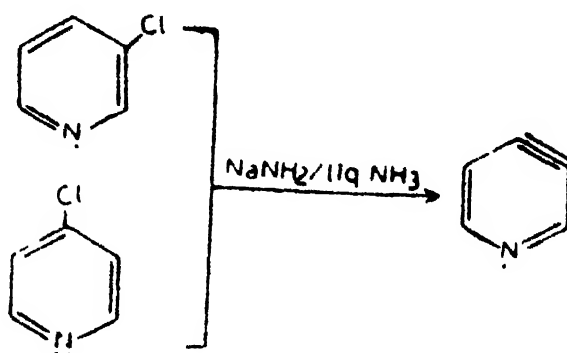
Pyridine N—oxide undergoes electrophilic substitution rather readily at the 4—position.

5. Pyridine being a tertiary amine forms quaternary salts 1-alkylpyridinium iodides with alkyl halides. The salt on heating, forms HI salt of α -picoline. The pyridinium salts are more reactive towards nucleophilic reagents than pyridine itself.

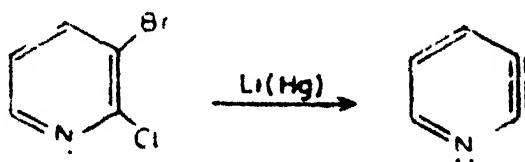


6. *Hetaryne Formation:* A *hetaryne* is an intermediate with a triple bond in the nucleus containing the hetero atom. The corresponding intermediate *benzyne* or *dehydrobenzene* is an intermediate in certain reactions of aromatic compounds. Only one type of dehydrobenzene is known but there are two *hetarynes* possible. The 3,4—hetaryne is obtained by the reaction of

NaNH_2 in liq. ammonia on 3— or 4—halopyridines. The corresponding 2,3—heteroalkyne cannot be obtained from 2—halopyridine because of amination



reaction. Instead it is obtained from 3—bromo—2—chloropyridine by treatment with Li amalgam



Uses

Pyridine finds uses as a solvent because of its high solvation properties, as catalyst in acylation, in denaturing alcohol and in the manufacture of dyes.

23.4 FUSED RING SYSTEMS

Of the fused ring systems we will discuss quinoline, isoquinoline, and purine. Fused systems, as discussed earlier have two atoms in common

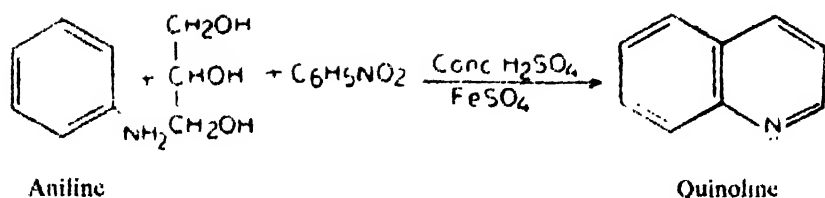
23.4.1 Quinolines

In quinoline, one benzene and one pyridine ring are fused together at the *ortho* positions. Quinoline was first isolated from coal tar and shortly afterwards from the distillation of quinine with alkali. It does not occur free in nature but many alkaloids derived from this ring system are well known, such as quinine, chloroquin, atarbrine, etc.

Preparation

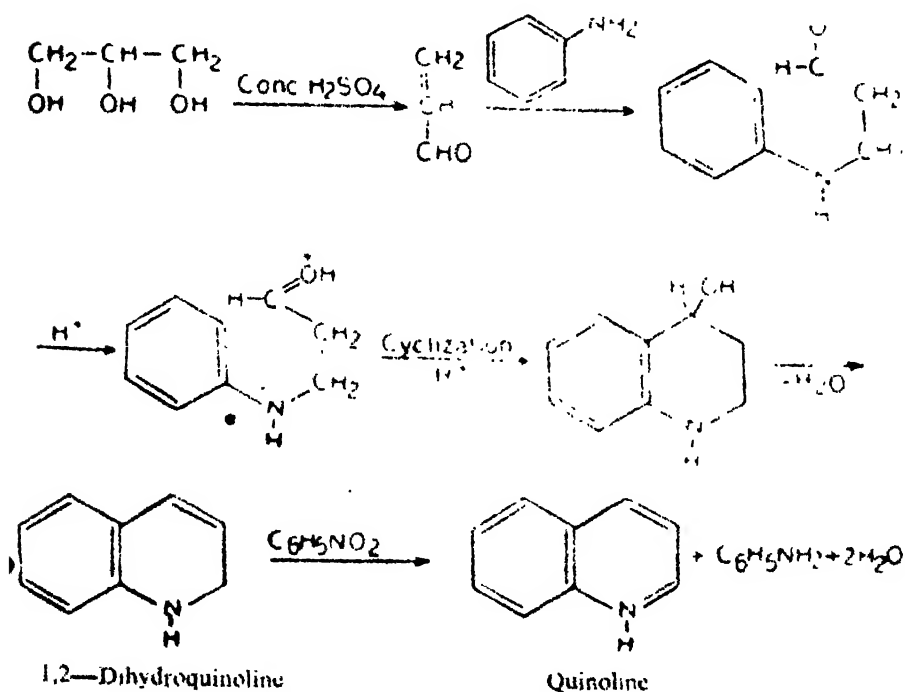
Quinoline is prepared by the following two methods:

1. *The Skraup Synthesis*: This is the commercial method for the preparation of quinoline. Aniline is heated with glycerol and conc. sulfuric acid in the presence of nitrobenzene as oxidizing agent.

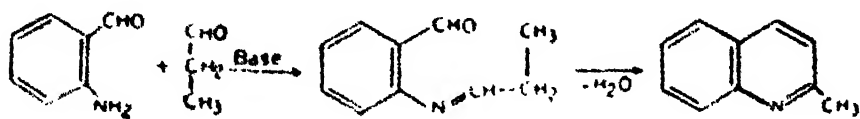


Mechanism

The first step involves the dehydration of glycerol to acrolein which condenses with aniline to form 1,2-dihydroquinoline which is oxidized to quinoline. Ferrous sulfate is used to slow down the otherwise vigorous reaction. 8-Hydroxyquinoline (oxine) is available by this method using *o*-aminophenol.

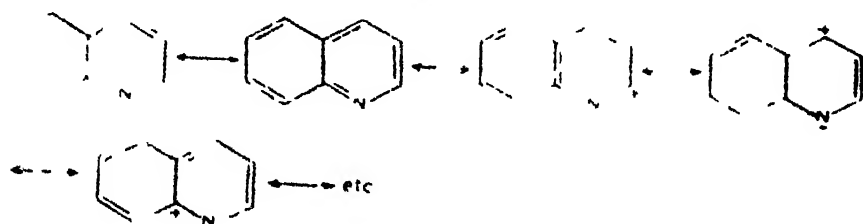


2. The Friedlander Synthesis: This method involves the alkaline condensation of *o*-aminobenzaldehyde with a carbonyl compound containing the grouping CH_2CO , i.e., having a reactive methylene group adjacent to the carbonyl group.



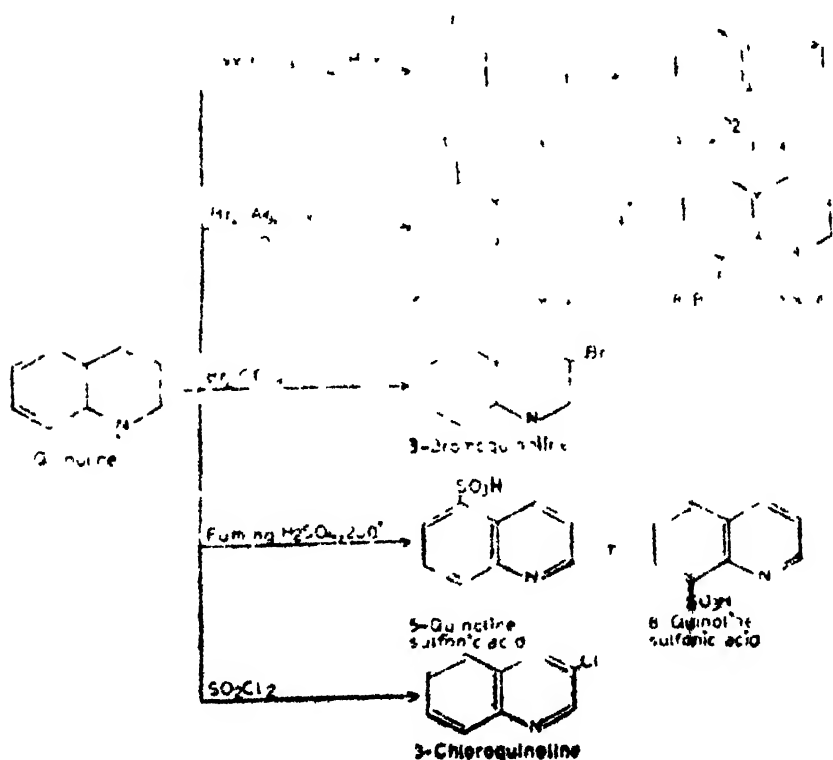
Properties

Quinoline is a colorless liquid, b.p. 237° . The lone pair is not involved in the aromatic sextet; it is thus mildly basic, the basicity being of the same order as that of aniline. The following resonance structures are important:



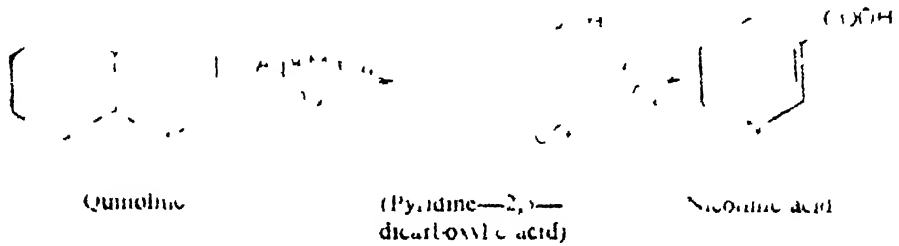
It possesses a resonance energy of 47.3 kcal/mole. The properties of the heterocyclic ring resembles those of pyridine.

1. *Electrophilic Aromatic Substitution*—Of the two rings in quinoline the benzene ring is electron rich. The electrophilic attack thus takes place in this ring at the 5- and 8-positions to give a mixture of products:

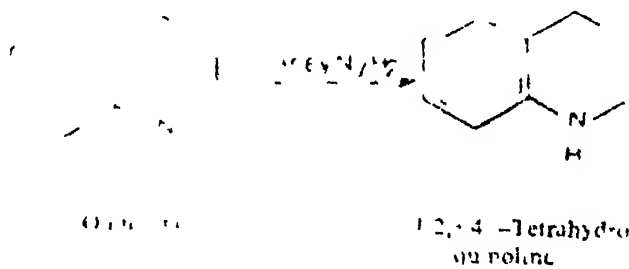


2. Oxidation with potassium permanganate opens the benzene ring to give pyridine-2,3-dicarboxylic acid, which decarboxylates to nicotine

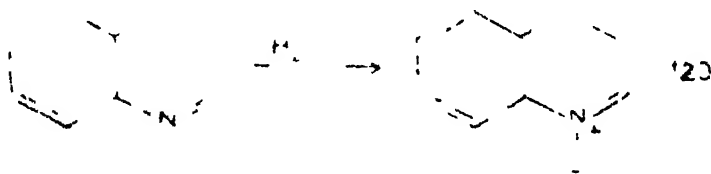
acid. Since pyridine ring is π -deficient and oxidation is dependent on the electron availability. The pyridine ring thus remains intact



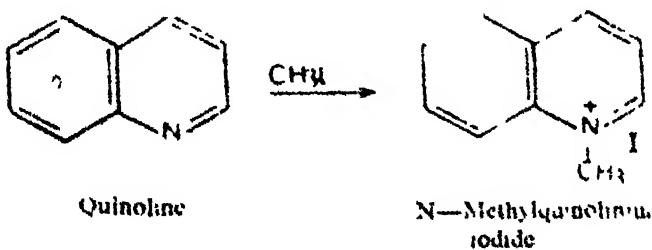
3. *Reduction* Chemical reduction of the pyridine ring is relatively easy but that of the benzene ring is difficult, it would be expected that the pyridine ring in quinoline would be more easily reduced.



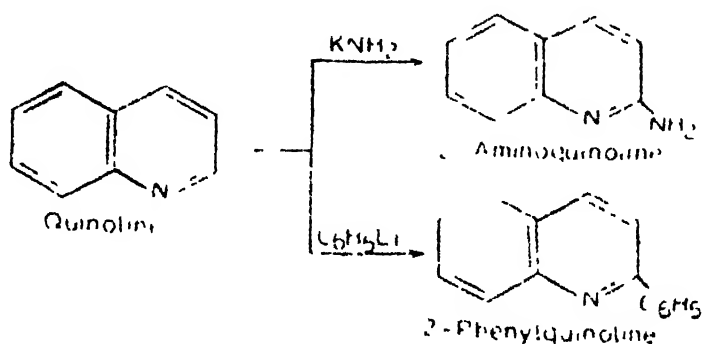
A mild oxidizing agent like hydrogen peroxide forms Quinoline N-oxide



1. Quinoline is a tertiary base and forms quaternary salts with alkyl halides. Quaternization assists the ability of quinoline to react with nucleophiles.



5. Quinoline undergoes nucleophilic substitution in a manner similar to pyridine. With phenyllithium, the 2-position is metallated which subsequently forms 2-phenylquinoline.



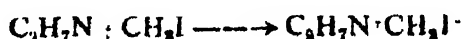
Constitution of Quinoline

The following facts and reasoning resulted in the elucidation of the structure of quinoline.

1. The molecular formula of quinoline as determined by analytical data and molecular weight determination is found to be $\text{C}_8\text{H}_7\text{N}$.

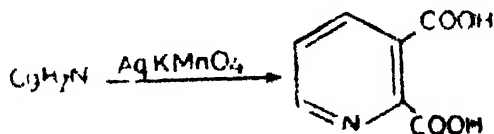
2. Quinoline undergoes electrophilic aromatic substitution, i.e. nitration, sulfonation and bromination, as do benzene and pyridine. This implies that there must be at least one aromatic ring present in quinoline.

3. Quinoline forms a quaternary ammonium salt with methyl iodide which suggests the presence of a tertiary nitrogen atom.

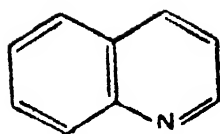


4. Valuable information about the structure of quinoline has been obtained by its oxidation reactions.

Oxidation of quinoline with KMnO_4 yields quinolinic acid. Naphthalene, on similar oxidation forms phthalic acid. It may thus be assumed that in



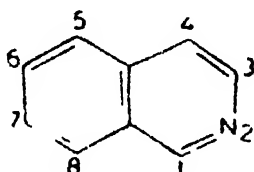
quinoline one benzene and one pyridine rings are fused together. The structure of quinoline may thus be postulated as follows:



This structure assignment has been confirmed by its independent synthesis as given earlier

23.4.2 *iso*-Quinolines

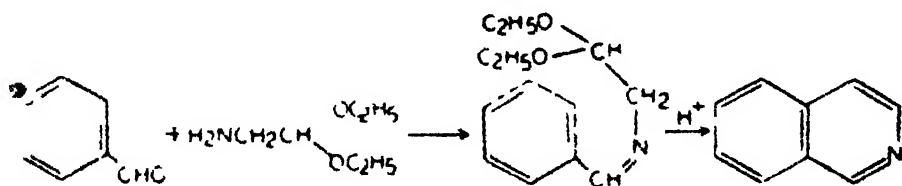
Isoquinoline occurs in coal tar and contains a benzene and a pyridine ring fused together. It is one of the very few heterocyclic compounds in which the numbering does not start at the hetero atom. The numbering rather commences adjacent to the benzene ring as in quinoline and naphthalene.



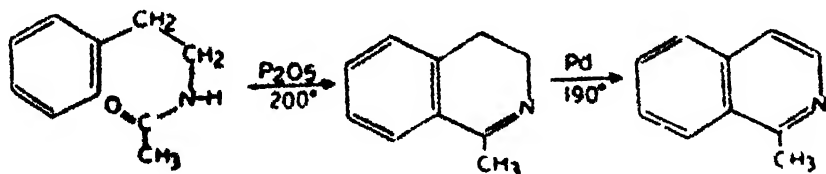
There are no *iso*-quinoline derivatives known as potential drugs. This ring system though occurs in several alkaloids.

Preparation

1 *The Pomeranz-Fritsch Synthesis* In this procedure a Schiff's base is first obtained between the reaction of an aromatic aldehyde and an iminoacetal. Cyclization is then accomplished in the presence of a catalytic amount of an acid to give *iso*quinoline.



2 *The Bischler-Napieralski Synthesis* An acyl derivative of β -phenylethylamine is treated with a dehydrating agent to form dehydro *iso*-quinoline which on dehydrogenation forms *iso*quinoline.

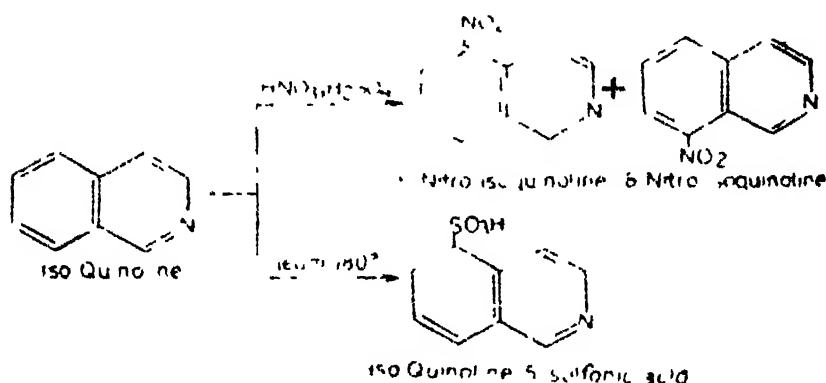


1-Methyl *iso*-quinoline

Properties

iso-Quinoline is a colorless liquid, b.p. 243°. It is fairly basic ($pK_b = 5.1$), several alkaloids like papaverine are based on the structure of *iso*-quinoline. It resembles quinoline in its chemical behavior.

1. **Electrophilic Aromatic Substitution:** Analogous to quinoline, the electrophilic attack in *iso*-quinoline takes place in the benzene ring due to the deactivation of the pyridine ring because of protonation



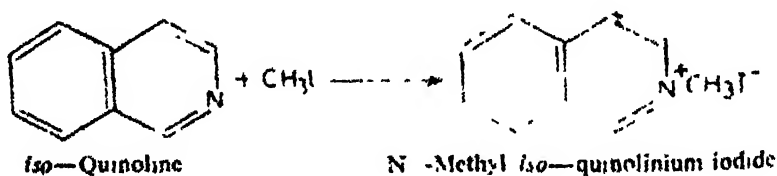
It is interesting to note that though positions 1 and 3 are adjacent to the nitrogen atom one might expect these positions to show electrophilic reactivity as displayed by the 2- and 4-positions in quinoline. However position-1 is activated towards electrophilic attack while position-3- is not. Attack at position-3 will result in the following charged form:



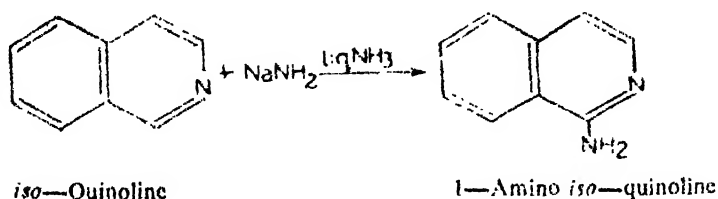
This would be of a very high energy as it contains the unstable *o*-quinone system and thus would not contribute to the resonance hybrid. As in the case of naphthalene it may be explained by saying that there is very little double bond character between $C-2$ and $C-3$ as between $C-1$ and $C-2$.

5-Bromo *iso*-quinoline is formed on reaction with $Br_2/AlCl_3$ while the 4-isomer is obtained with Br_2/CCl_4 .

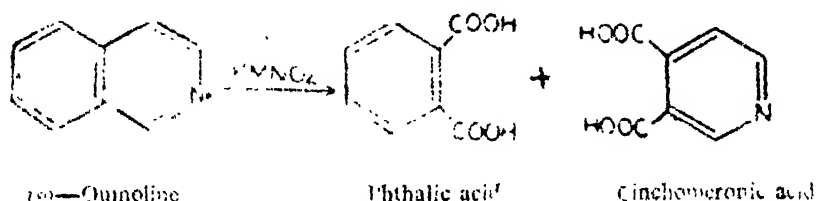
2. With alkyl halides, *iso*-quinoline forms a quaternary salt



3. *iso*-Quinoline undergoes the usual Chichibabin reaction with sodamide in liq NH_3 .

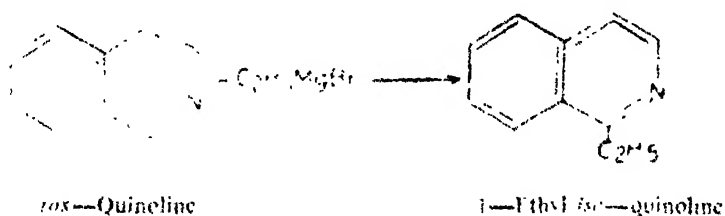


4. *Oxidation*: A strong oxidizing agent leads to the formation of equal amounts of phthalic acid and cinchomeronic acid, while it is resistant to the attack of most oxidizing agents.

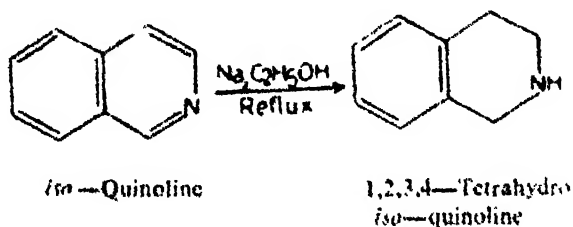


The action of perbenzoic acid converts *iso*-quinoline into its N-oxide.

5. With Grignard reagent a nucleophilic attack of the Chichibabin type takes place on *iso*-quinoline.

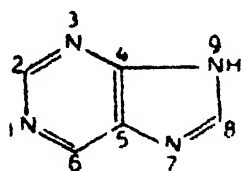


6. *Reduction*: Similar to quinoline, the pyridine ring in *iso*-quinoline is also reduced more rapidly than the benzene ring



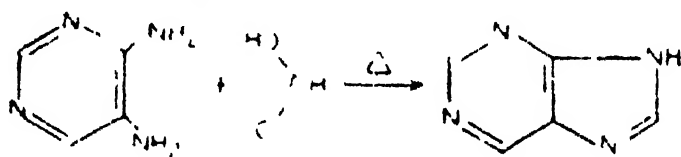
23.5 PURINES

The purine ring system is one of the most important present in living systems and is formed from the fusion of a pyrimidine and an imidazole ring. The purine ring system is present in many natural products and in nucleotides obtained by hydrolysis of nucleic acids. Though there is no rigid classi-

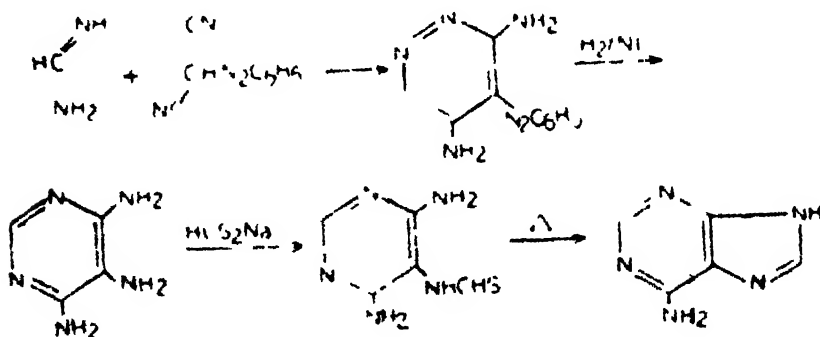


Purine

fication of purines, they may be divided into two types namely hydroxypurines (having hydroxyl group), i.e., uric acid, xanthine and aminopurines (having amino group), i.e., adenine, guanine. The parent compound purine was synthesized by heating 4,5-diaminopyrimidine with formic acid.



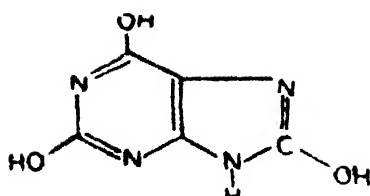
Adenine is obtained from formamidine and phenylazomalonnitrile in the following steps



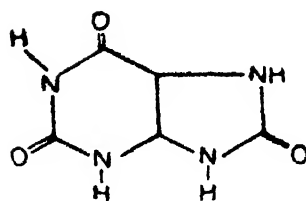
Purine is a colorless compound, m.p. 212°, and is soluble in water but sparingly soluble in organic solvents. Purine is a stronger base ($pK_b = 2.4$) than pyrimidine ($pK_b = 1.3$).

23.6 URIC ACID (2,6,8-Trihydroxypurine)

Uric acid is a member of the purine family. It occurs in two tautomeric forms, i.e., lactim and lactam forms.



Lactim form



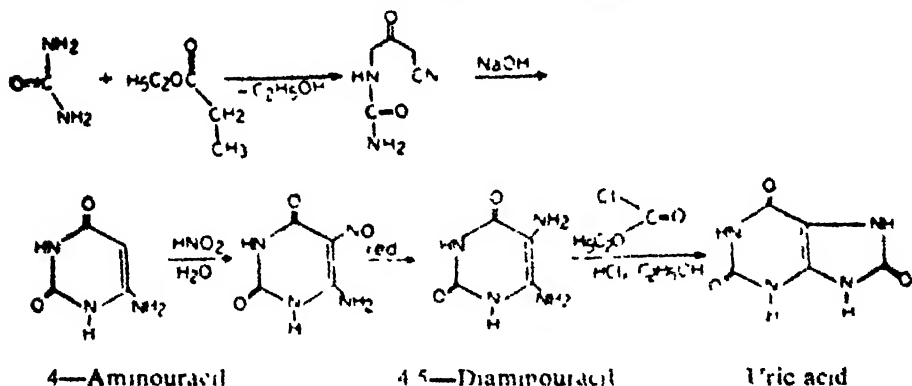
Lactam form

Uric acid is a component of urine and is the major nitrogen-containing excretion product of birds and reptiles. In the disease *gout*, the rate of formation of sodium urate is increased and crystals of this salt precipitate in joints causing painful inflammation and leading to arthritis. Kidney stones may also form.

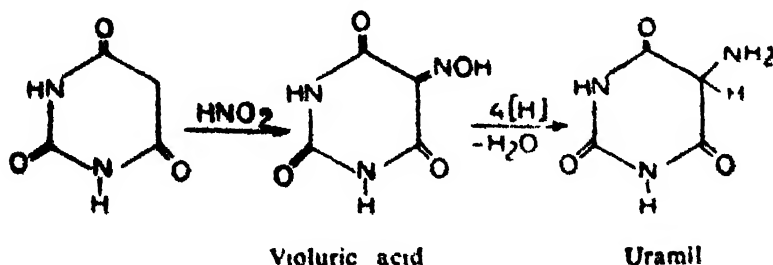
Preparation

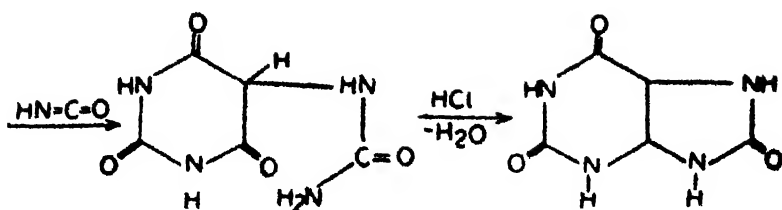
Uric acid may be prepared by the following two methods:

1. *The Traube Synthesis*: In this method, urea is condensed with ethylcyanoacetate to give cyanoacetylurea. This intermediate is cyclized to 4-aminouracil by alkali. This latter compound is then nitrosated, reduced and then converted into the corresponding urthane by treating with ethylchloroformate. Urethane, on warming loses C_2H_5OH to yield uric acid.



2. *The Fischer Synthesis*. Barbituric acid is treated with nitrous acid to yield the oxime of alloxan (violuric acid) which is then reduced to 5-amino-barbituric acid (uramil). The latter is heated with KCN to give pseudouric acid and then to uric acid by heating with hot conc. HCl.

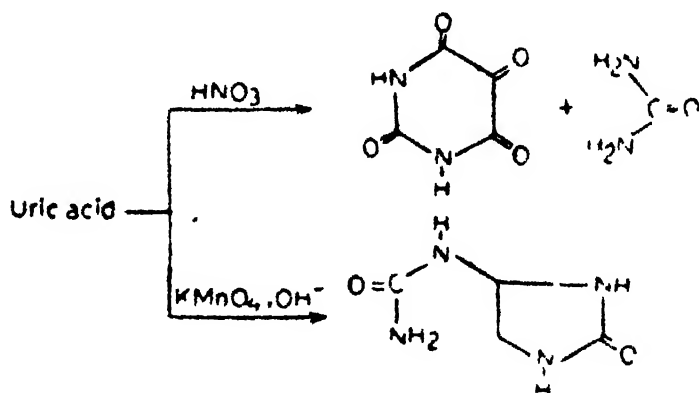




Properties

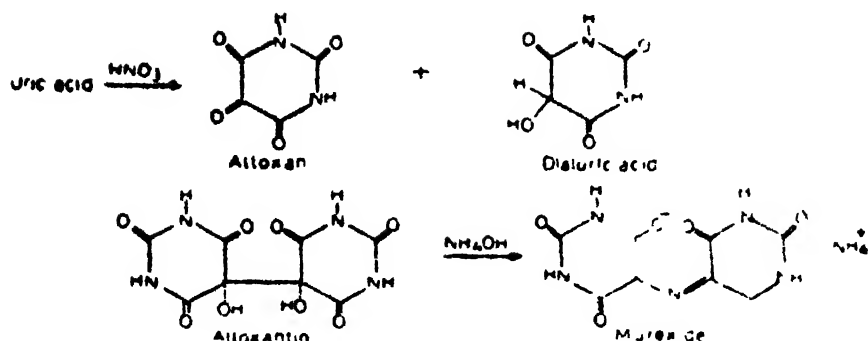
Uric acid is a white crystalline compound, sparingly soluble in hot water. It exists in two forms out of which the lactam form predominates. It behaves as a weakly dibasic acid and forms two series of salts, the acids and neutral urates in which one or two hydrogen atoms have been replaced by a metal.

Uric acid undergoes oxidative degradation with nitric acid to alloxan and urea, and with alkaline permanganate to allantoin.



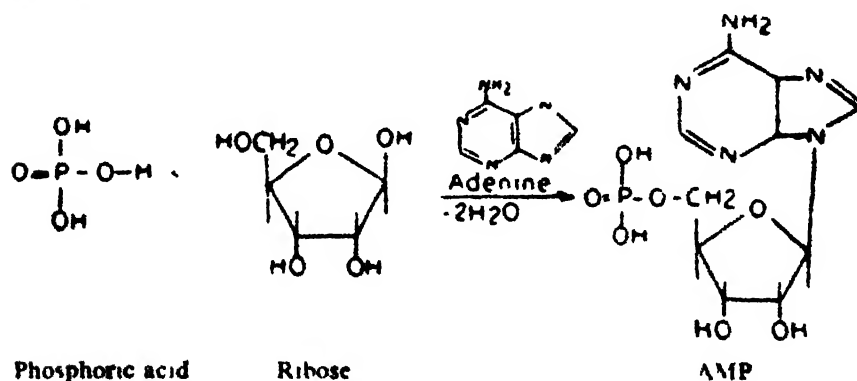
This degradation was the key step in the establishment of structure for uric acid.

An analytical test for uric acid is the appearance of a purple color on adding ammonia to the residue obtained by evaporating the solution of a small amount of uric acid in nitric acid. The color appears due to the formation of murexide. Oxidation of uric acid first results in alloxan and dihydrouric acid which condense to alloxantin. This is then converted to murexide with ammonia. Murexide is used as an indicator in complexometric titrations.

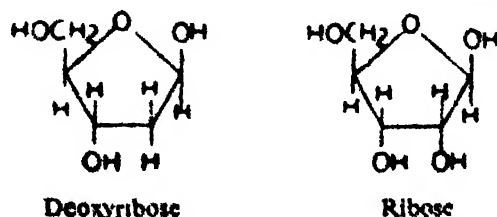


23.7 NUCLEIC ACIDS

Nucleic acids are biomolecules and play an important role in the storage of genetic information and in the biosynthesis of proteins. Nucleic acids occur in every living cell and like proteins they are polymers of high molecular weight. There are two types of nucleic acid—deoxyribonucleic acid (DNA) a constituent of the nucleus and ribonucleic acid (RNA), present in the cytoplasm outside the nucleus. The monomer unit of these biopolymers is called a *nucleotide*. Unlike the monomer unit of other polymers, a nucleotide can be hydrolyzed. Base hydrolysis of a nucleotide leads to a nitrogenous base (a derivative of purine or pyrimidine), a five-carbon sugar D-ribose and phosphoric acid. The assembly of a typical nucleotide, adenosine monophosphate (AMP) is shown below.

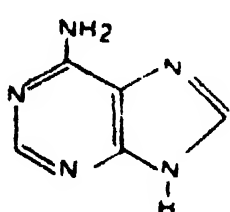


The nucleotides of DNA are built from deoxyribose (*deoxy* means lacking in an oxygen atom) and those of RNA from ribose.

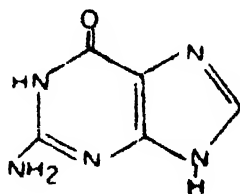


Both DNA and RNA consist of a long chain alternating sugar and phosphate residues

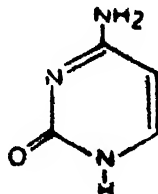
Hydrolysis of nucleic acids yields five heterocyclic bases. Three are common to both DNA and RNA—adenine, guanine and cytosine



Adenine

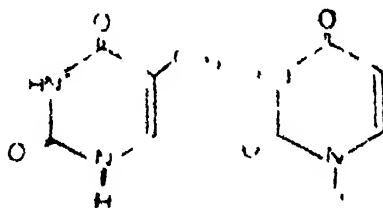


Guanine



Cytosine

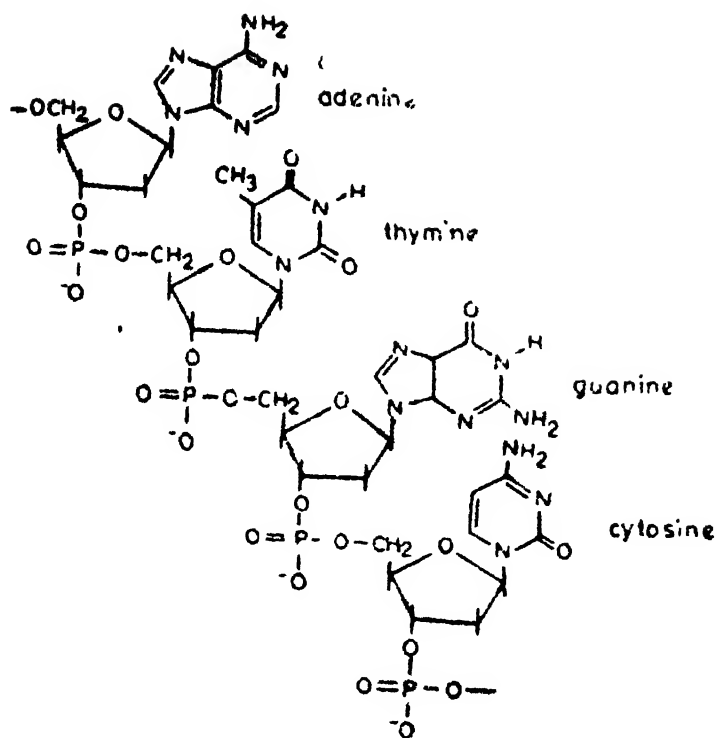
Of the remaining two—thymine is found only in DNA, while uracil only in RNA.



Thymine

Uracil

Various nucleotides combine by the loss of a molecule of water from the phosphoric acid unit of one nucleotide with an alcohol unit of the sugar residue of the next molecule. This gives rise to a phosphate ester linkage. This process is repeated until hundreds of nucleotide units are incorporated into the polymer. A segment of deoxyribonucleic acid (DNA) is shown below:



A typical DNA strand

The backbone of a nucleic acid consists of regularly alternating phosphate and pentose units. The heterocyclic bases are linked to C—1 of each pentose unit whereas the phosphate group of one nucleotide is joined with the C—3 atom of the ribose (or deoxyribose) unit of the succeeding nucleotide.

The structure of DNA has been described as a double-stranded helix comprising of two DNA chains twisted together in a helical fashion. The two chains are held together by hydrogen—bonds between pairs of bases in the two chains. A thymine unit of one chain pairs with adenine of the other chain *via* hydrogen bonds and guanine with cytosine. Genetic information is passed from cell to cell in a process called DNA replication. A *gene* is a section of a DNA molecule that is 'coded' for a specific genetic message. Since the DNA molecules have the same backbones, the differences in life functions related to it are based on the sequence and kind of bases on the nucleic acids. It is this sequence of bases, which is generally accepted as a *genetic code* in which biological information is recorded in a nucleic acid molecule.

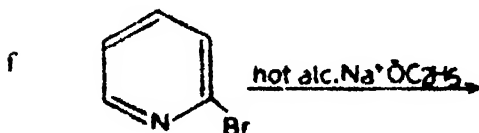
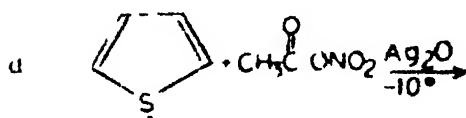
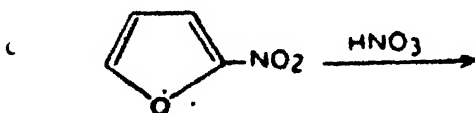
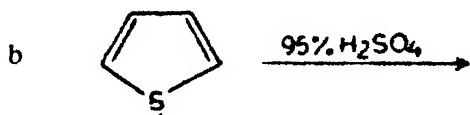
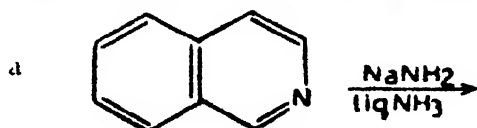
The first gene to be made artificially, but functional in a living cell (a bacterium) was announced by Nobel laureate, H.G. Khorana in 1976.

RNA differs from DNA in that the sugar unit is deoxyribose in case of DNA. RNA exists as single strand, unlike DNA. RNA can be of three

types Ribosomal RNA constitute the major amount of RNA and are also called *ribosomes*. They perform a structural function. *Messenger RNA* account for about 5–10% of the total RNA cell, and function as a template for the synthesis of proteins. *Transfer RNA*, or soluble RNA are the smallest of the RNAs. Being small they are more soluble and more mobile. They are also involved in protein synthesis, in the transfer of amino acids from solution to the growing protein chain.

QUESTIONS

- 23.1 By drawing resonance structures show why the attack of NO_2^+ takes place at the 2— and not the 3—position in thiophene.
 23.2 Write products of the following reactions:

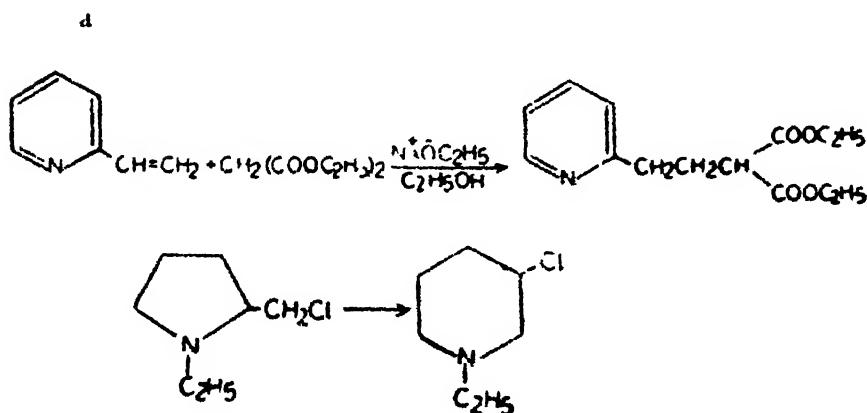


- 23.3 Describe the preparation and properties of furan.
 23.4 Write structure formula for the following compounds

- a 2—Methylquinoline
 b β —/—Butylpyridine

- c. α -Methylthiophene
- d. β -Chlorofuran
- e. 2,5-Diaminopyridine
- f. 3-Nitropyrrole
- g. 8-Nitro *iso*-quinoline
- h. Furil
- i. Furilic acid
- j. Furom

- 23.5 Write short notes on the Chichibabin and Vilsmeier reactions.
- 23.6 Compare the basicity of pyrrole and pyridine. Draw their molecular orbital diagrams.
- 23.7 Propose mechanisms for the following reactions.



- 23.8 A tertiary amine $C_9H_{19}N_7$ was subjected to Hofmann degradation to give an unsaturated amine. This amine on further Hofmann degradation yielded a diene C_8H_{14} and a tertiary amine. Oxidation of the diene with $KMnO_4$ led to formic, propionic and acetic acids in a molar ratio of 1 : 1 : 2. Ozonolysis of the diene led to mixture of $HCHO$, CH_3CH_2CHO and 2,3-butanediene. Write the structures of all the unknown compounds.
- 23.9 Why does an electrophilic attack in quinoline take place on the benzene ring?
- 23.10 Although the 1- and 3-positions are both *ortho* to a 2-substituent in the naphthalene series, the two positions exhibit different chemical properties. Illustrate how a similar difference exists in the isoquinoline series, using an appropriate reaction. Offer an explanation for the difference.

- 23.11 Discuss in brief the constitution of any two of the following:
- Quinoline
 - Thiophene
 - Pyridine
- 23.12 How is pyridine obtained from coal tar? Describe two methods for its preparation. How does it react with:
- Bromine
 - Conc H_2SO_4
- 23.13 Give two methods employed for the preparation of pyrrole. In what respects does it resemble an aromatic substance?
- 23.14 What are heterocyclic compounds and how are they classified? Give important properties of pyridine and discuss its constitution.
- 23.15 Describe two methods for the synthesis of pyridine. Compare and contrast its properties with that of benzene. Give the chief uses of pyridine.
- 23.16 How will you synthesize the following:
- Pyrrole from acetylacetone
 - Furan from 1,4-diketone
- 23.17 Compare the basicity of pyridine with that of pyrrole and justify your conclusion on the basis of their structure.
- 23.18 How will you arrive at the structure of pyridine?
- Explain electrophilic and nucleophilic substitution in pyridine with the help of an example in each case.
 - Is pyridine soluble in water? Explain.
- 23.19 Describe the synthesis of quinoline and discuss its structure.
- 23.20 Write a short note on the synthesis of quinoline and isoquinoline.
- 23.21 Explain the following:
- Electrophilic substitution of pyrrole is easier than in the case of benzene.
 - Electrophilic substitution of pyridine is difficult to achieve.
 - Pyrrole is less basic than pyridine.
 - Electrophilic substitution of pyridine is similar to nitrobenzene.
 - Electrophilic attack in thiophene takes place 2-position.
 - Furan undergoes Diels-Alder reaction readily.
 - Nitration in iso-quinoline takes place at 5-position.
 - Pyridine undergoes nucleophilic substitution rather easily.

- i. Furan participates in the D—A reaction more readily than pyrrole.
- 23.22 What are nucleic acids? Can they be considered polymers. Name the two types of nucleic acids and write the structures of their monomers.
- 23 23 Show all the steps for the synthesis of 2—methylquinoline according to the Skraup procedure

Carbohydrates

A variety of compounds obtained from natural sources will be discussed in this and the following chapters. These compounds include carbohydrates, alkaloids, amino acids, proteins and terpenes. These classes of natural products are important biologically and essential to sustain life. Some of these provide the organism with the necessary energy (carbohydrates and proteins), others have various physiological effects (alkaloids), while some are important from the medicinal point of view (terpenes).

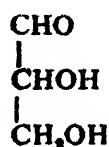
Carbohydrates (saccharides) occur naturally in the animal and vegetable kingdom. These, along with fats and proteins, form the basis of animal nutrition. Sugars, starches and cellulose are probably the best known members of this group. Carbohydrate moieties also occur in a number of complex materials such as glycosides, mucoproteins, nucleic acids, etc. Chemical analysis of sugar and other carbohydrates show that they are composed only of carbon, hydrogen and oxygen and their general formula can be expressed as $C_x(H_2O)_x$, e.g., $C_6H_{12}O_6$ or $C_6(H_2O)_6$ and $C_{12}H_{22}O_{11}$ or $C_{12}(H_2O)_{11}$, etc., i.e., they appear to be hydrates of carbon. The carbohydrates usually contain hydroxyl, ether or carbonyl functions. According to the modern definition of *carbohydrates* they are polyhydroxy ketones or aldehydes or substances that yield such products on hydrolysis. Low molecular-weight carbohydrates are called sugars or saccharides. A sizeable part of the chemistry of carbohydrates deals with the reactions of aldehydes and ketones. The name carbohydrate has survived since its inception by Schmidt in 1844 though it has no chemical meaning. The names of the individual sugars are characterized by the ending *-ose*. Carbohydrates are stored as glycogen in the body.

24.1 CLASSIFICATION OF CARBOHYDRATES

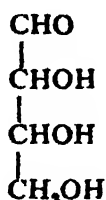
For the sake of convenience the carbohydrates are divided into three main groups according to their molecular structure and physical and chemical properties.

Monosaccharides: These are the simplest carbohydrates and also called simple sugars. They cannot be hydrolyzed further into simpler sugars. The

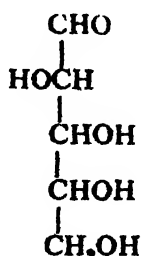
most important of them are the *pentoses*, $C_5H_{10}O_5$, and the *hexoses*, $C_6H_{12}O_6$. The monosaccharides are further subdivided in terms of the number of carbon atoms and the nature of the carbonyl groups present in the molecule. If an aldehyde group is present, it is known as an *aldose* and a *ketose* if a keto group is present in the chain. A three carbon chain is called an *aldotriose* or *ketotriose*, a four carbon atom chain as *aldotetrose* or *Ketotetrose* and so on. Examples of each kind are given below:



D—Glyceraldehyde
(An aldotriose)



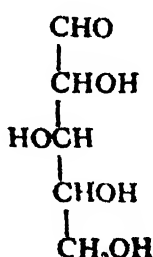
D—Erythrose
(An aldotetrose)



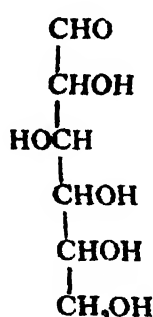
D - Arabinose
(An aldopentose)



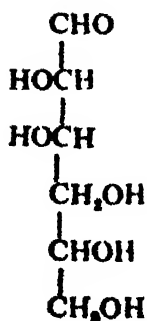
D—Ribose
(An aldopentose)



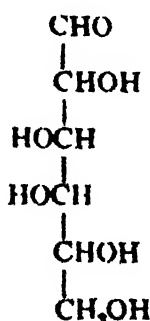
D—Xylose
(An aldopentose)



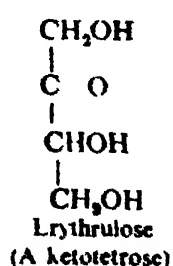
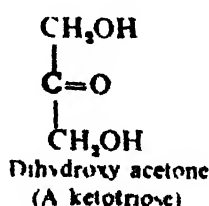
D—Glucose
(An aldohexose)

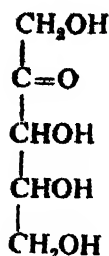


Mannose
(An aldohexose)

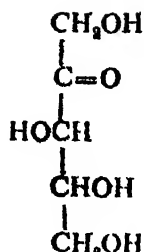


D—Galactose
(An aldohexose)

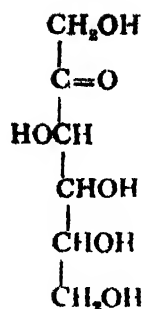




Ribulose
(A ketopentose)



Xylose
(A ketopentose)



D—Fructose
(A ketohexose)

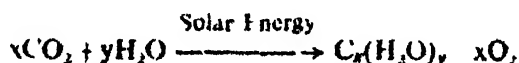
Disaccharides: These are composed of two monosaccharide molecules bonded together by ether linkages and may be hydrolyzed to yield the constituent units. Sucrose, for instance, on hydrolysis yields glucose and fructose. They are crystalline solids, soluble in water and sweet in taste. Representative examples are, Cane sugar, lactose, cellobiose and maltose.

Oligosaccharides: This is a general term used to describe sugar polymers containing upto eight monosaccharide units. They include disaccharides, trisaccharides, tetrasaccharides, etc.

Polysaccharides: These are composed of several monosaccharide units and are polymers. On hydrolysis they yield a large number (> 10) of monosaccharides. Starch on hydrolysis gives several molecules of glucose. These are non-sugars, insoluble in water and are the most abundant form of carbohydrates. Important examples include starch and cellulose.

24.2 OCCURRENCE OF CARBOHYDRATES

Carbohydrates are ultimately derived from the reduction of carbon dioxide, by living plants with the aid of the green pigment, *chlorophyll*. The energy



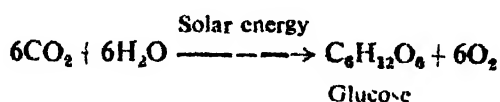
is obtained from sunlight and this process is known as *photosynthesis*. Glucose and fructose occur in grape juice, and sugar (sucrose) occurs in sugarcane and beets. Lactose is present in cow's milk. Starch is obtained from potatoes, corn cobs and many plants, whereas cellulose is a major constituent of wood. It is also the principal component of cotton.

24.3 MONOSACCHARIDES

The monosaccharides are those carbohydrates which cannot be further degraded by hydrolysis. They include both aldoses and ketoses. The most important sugars of this class are glucose and fructose.

24.3.1 Glucose

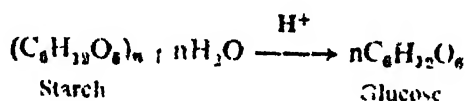
The name glucose is derived from a Greek word for *sweet wine* and reflects the fact that it was originally isolated from grapes. Glucose, because of its origin, is sometimes called *grape sugar*. The alternative name *dextrose* originated from the fact that the common form of the sugar rotates the plane of polarized light to the right, i.e., it is *dextro* rotatory. Glucose is the most widely occurring monosaccharides in nature and occurs free in fruit juices, honey and is also obtained by the hydrolysis of starch and cellulose. It is the final product of *photosynthesis*, i.e., the process in which plants produce oxygen by utilizing carbon dioxide and water.



Glucose is involved in the metabolic activities of living organisms and is formed by the hydrolysis of sucrose and starch. In the blood stream a definite concentration of glucose must be maintained because both, an excess and a deficiency, are fatal for the organisms. Excess glucose is excreted in the urine. The concentration of glucose in the body is maintained by the action of hormones (insulin)

Preparation

Glucose is obtained on a commercial scale from the hydrolysis of starch in the presence of a mineral acid. In practice, the starchy material is mixed

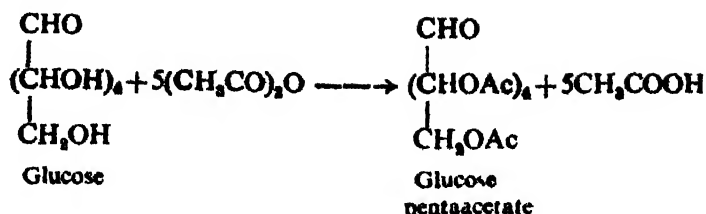


with twice its weight of water and dil. sulfuric acid. The mixture is heated under pressure. When the hydrolysis is complete, the excess acid is neutralized with CaCO_3 and filtered. The clear filtrate is decolorized with animal charcoal, filtered again and finally concentrated. Glucose crystals separate on cooling.

Properties

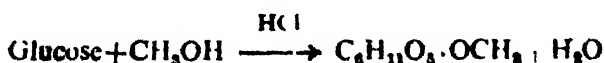
Glucose is a white crystalline powder and is highly soluble in water. It undergoes the following important chemical reactions

1. **Esterification:** The hydroxyl groups in glucose can be esterified with acetic anhydride to give a pentaacetyl derivative.



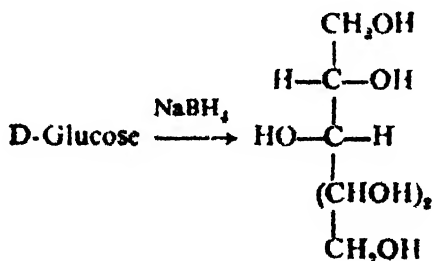
The reaction has been useful for elucidating the structure of glucose.

2. *Formation of Glucoside*: When glucose is dissolved in alcohol and the solution treated with a mineral acid, a cyclic ester results acquiring only one methyl group. In carbohydrate chemistry such a compound is termed as *glycoside* and a glycoside derived from glucose is termed as *glucoside*. The aldehyde function disappears in a glycoside. Since a methyl group is



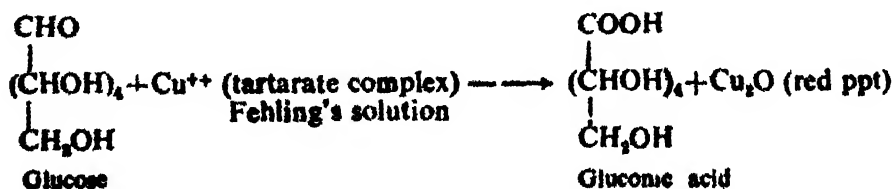
transferred to the oxygen atom, the process is termed as *methylation*. Only one equivalent of methanol reacts to give the hemiacetal type compound.

3 *Reduction*. Monosaccharides may be reduced by different methods to the corresponding polyalcohols, which as a class are called *alditols*. Reduction of D-glucose with NaBH_4 gives D-glucitol (referred to as sorbitol in older literature)

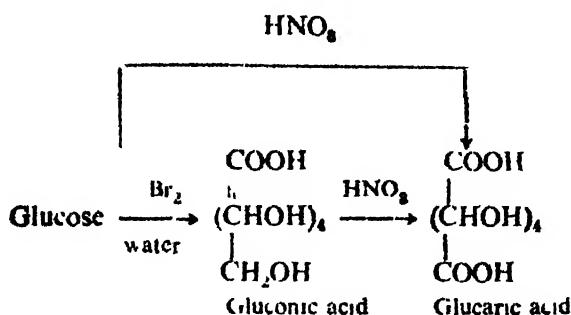


4. *Oxidation*: Mild oxidizing agents such as Fehling's solution, Tollens' reagent and Benedict's solution oxidize an aldose to an aldonic acid while nitric acid oxidizes it to an aldonic acid.

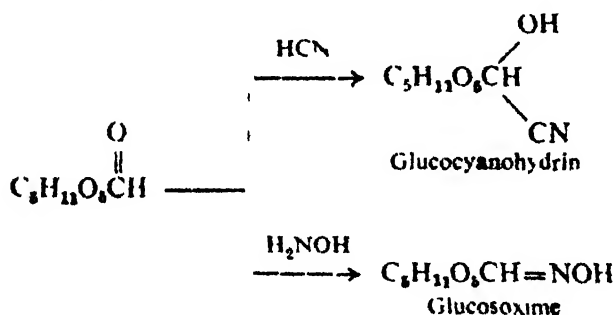
Since glucose gives a positive test with all these reagents, it is also called a *reducing sugar*.



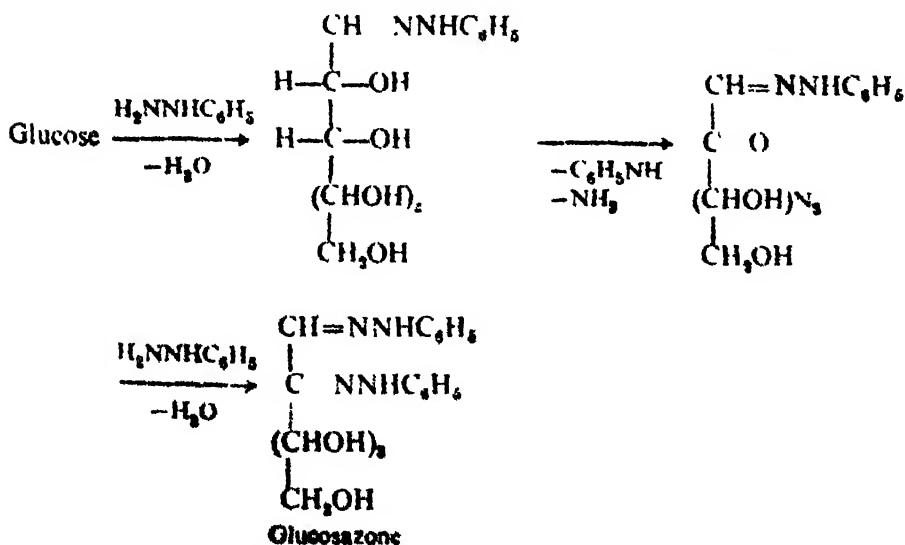
Bromine water (hypobromous acid) oxidizes glucose to aldonic acid which is further oxidized by nitric acid to glucaric acid, a dicarboxylic acid. Direct oxidation of glucose by nitric acid also leads to the same acid.



5. Reactions of the Carbonyl Function: Glucose reacts with reagents like HCN, H_2NOH , $\text{C}_6\text{H}_5\text{NHNH}_2$, etc., in a manner typical of aldehydes.



In contrast, three molecules of phenylhydrazine react with glucose to form an osazone which is a bright yellow solid. The osazones are more easily



handled than the sugars themselves (sugars tend to form syrups when not completely pure).

Phenylhydrazine itself is a mild oxidizing agent and is capable of converting the adjacent —OH group to a keto group.

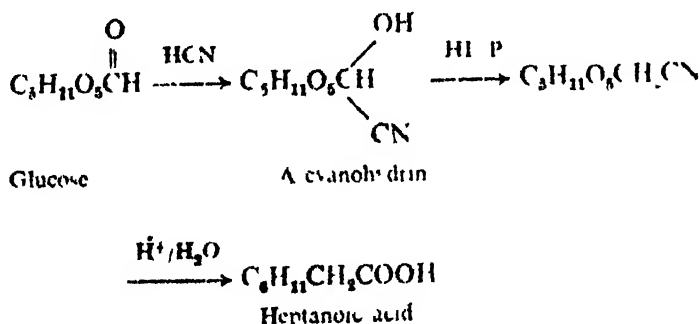
6. The open structure of glucose, although contains a —CHO group, differs in many respects from the normal aldehydes. For instance, glucose neither gives an adduct with NaHSO_3 , nor does it give pink color with Schiff's reagent. Instead, glucose responds to Molisch's test and mutarotates (see Sec. 24.4).

24.3.2 Constitution of Glucose

The elucidation of the structure of glucose is based on the following evidence.

1. Determination of molecular weight of glucose showed the molecular formula to be $\text{C}_6\text{H}_{12}\text{O}_6$.

2. *Presence of a Straight Chain:* One of the earliest experiments performed for the structural elucidation of glucose was a direct reduction. The glucose cyanohydrin on reduction with HI and subsequent hydrolysis yields heptanoic acid. This shows that the carbon atoms are arranged linearly



3. *Presence of an Aldehyde Group:* The presence of an aldehyde function has been based on several chemical reactions

- Glucose reacts with HCN and H_2NOH in the same manner as aldehydes do.
- The aldehyde group is oxidized with bromine water to a carboxyl function
- Glucose also responds to Fehling's and Tollens' tests.

The formation of an acid further indicates that the aldehyde group is present at the terminal carbon atom since only an aldehyde can be easily oxidized to an acid.

4. With acetic anhydride, glucose yields a pentaacetate derivative.

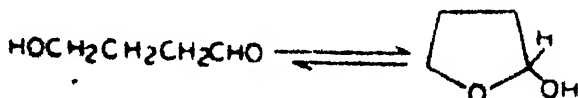
24.3.3 Cyclic Structure of Glucose

Though the open chain structure accounts for many properties of glucose, it fails to accommodate the following observations:

- Glucose contains a —CHO group but it does not condense with NaHSO_3 as aldehydes do.
- Two isomeric glucosides (α and β) can be obtained by heating D-glucose with methanol and a mineral acid.
- D-Glucose displays mutarotation, i.e., when dissolved in water, its specific rotation changes from $+113^\circ$ to an equilibrium value of $+52.5^\circ$. For L-Glucose, the value rises from 19° to 52.5° .

Tollens' (1863) concluded that the simple sugars do not exist in the form of aldehydes and ketones but as ring structures. There are two lines of evidence to support a cyclic structure.

First: Glucose reacts with just one equivalent of methanol to yield a mixture of acetal type products. This indicates that glucose itself might exist as a hemiacetal because it adds only one molecule of methanol. Ordinary aldehydes would require two molecules of methanol to form acetal. This is not surprising because compounds containing both an aldehyde and hydroxyl groups exist principally in a cyclic form, of the type shown below:

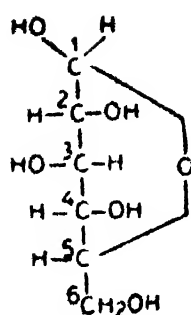
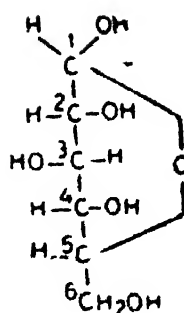


In glucose also, the aldehyde and hydroxyl groups interact to form a six-membered hemiacetal ring.

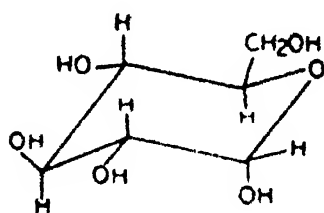
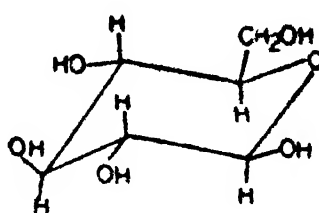
The reaction involves the migration of one hydrogen atom from an alcohol group to the carbonyl group with the formation of a bond between the oxygen of the alcohol and the carbonyl carbon to give a ring structure. When this happens, the carbonyl carbon (C_1) becomes asymmetric and two isomers are possible. These are called the α — and β —forms.

Second: Another indication of the cyclic nature of glucose comes from the observation of another phenomenon known as mutarotation.

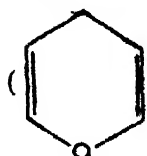
According to this the two forms of glucose L— and D—, attain an equilibrium value of optical rotation when dissolved separately in water even though they have different initial values. The explanation of mutarotation is that the sugar exists in solution as a mixture of two ring forms in equilibrium with a comparatively small proportion of glucose in the open—chain or aldehydic form. The cyclic structure thus can be represented as follows:

 α -D(+)-Glucose β -D(+)-Glucose

These two cyclic isomers differ only in the stereochemistry at carbon—1; such isomers are called *anomers*. The —OH in the α —form is written to the right while in the β —form it is to the left. Haworth described the structures by putting the substituents on a simple planar hexagon as shown below:

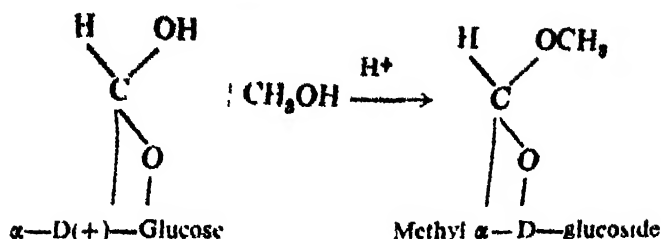
 α -D(+)-Glucopyranose β -D(+)-Glucopyranose

These are called the *Haworth projection* formula and are known as pyranoses because of the presence of a six—membered heterocyclic pyran ring



(). α -D—Glucose is thus also called α -D—glucopyranose and

β -D—glucose is called β -D—glucopyranose. When drawn in their chair conformations, the most stable conformation is that which has more of the bulky groups in equatorial positions. The pyran ring is not planar and the boat form is energetically less favorable. The assignment of a cyclic structure explains the formation of two glucosides on reaction with methanol.



Similarly the β -form reacts to give methyl- β -D-glucoside.

This concentration, however, is sufficient for glucose to show typical aldehyde reactions, yet is not sufficient for the Schiff's test.

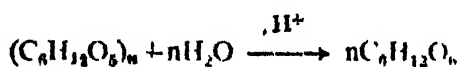
It may be noted that a glucoside cannot mutarotate because the alkoxy group cannot convert into an aldehyde group as a hydroxyl group can.

24.3.4 Fructose

This is the most abundant of the ketohexoses. The name fructose is derived from the Latin word for fruit, *fructus*, the other common name for this sugar is, *Levulose*, indicating its *levorotatory* property. Fructose is formed along with glucose in the hydrolysis of cane sugar. In the free state it occurs in fruit juices and honey and is sometimes also referred to as *fruit sugar*.

Preparation

It is obtained by hydrolysis of polysaccharides, inulin (obtained from *dahlia* bulbs) in the presence of a mineral acid. The excess acid is neutralized with

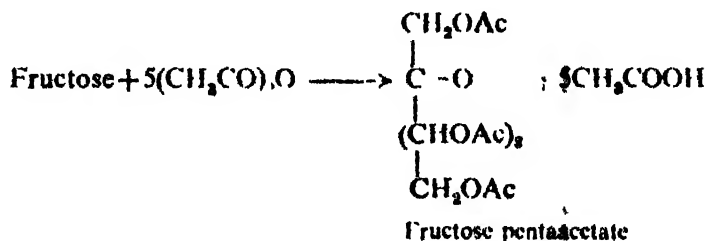


$\text{Ba}(\text{OH})_2$ and filtered. The clear filtrate is concentrated and allowed to cool, fructose crystallizes out

Properties

Fructose is a white crystalline powder and highly soluble in water.

1. *Esterification*: It forms a penta-acetyl derivative with acetic anhydride, as does glucose.



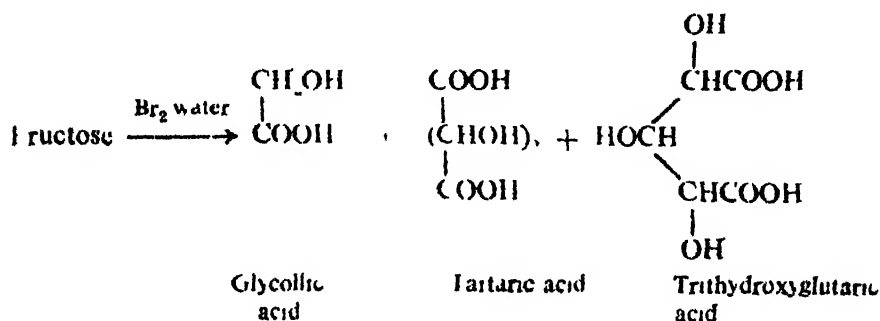
2. *Formation of Fructosides*: Analogous to glucose, fructose forms fructoside with CH_3OH and catalytic amount of hydrochloric acid.



2. *Reduction*: Reduction of D—fructose with NaBH_4 produces D—glucitol and D—mannitol.

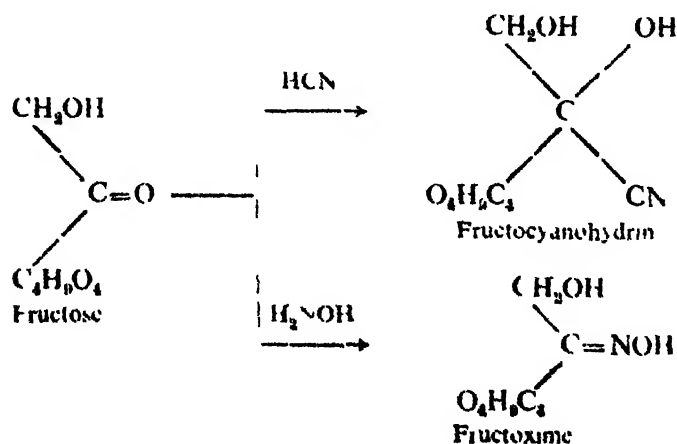


4. *Oxidation*: With bromine water fructose is oxidized to a mixture of carboxylic acids.

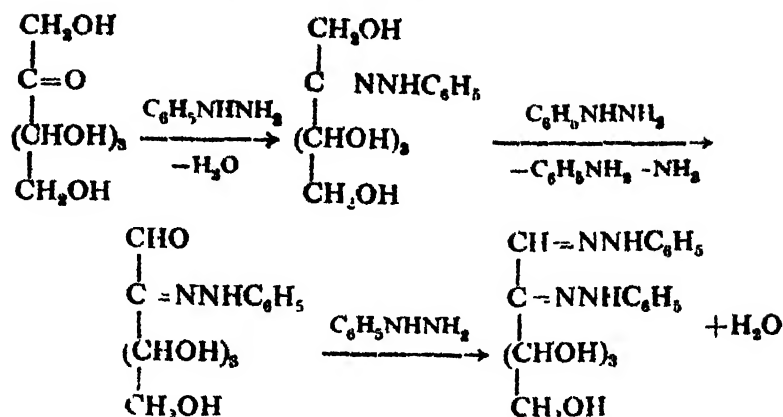


Fructose is a non-reducing sugar; unlike glucose it is not oxidized by Fehling and Tollens' reagents.

5. *Reactions of the Carbonyl Function*: Fructose reacts with HCN , H_2NOH and $\text{C}_6\text{H}_5\text{NHNH}_2$ in a manner similar to glucose.



Osazone formation takes place with three molecules of phenylhydrazine similar to glucose.



This osazone is identical to that formed from glucose.

6. Fructose, though it contains a keto group, differs from ketones in many respects, for instance, it does not add on NaHSO_3 and it mutarotates

24.3.5 Constitution of Fructose

1. The molecular formula of fructose from molecular weight determination is found to be $\text{C}_6\text{H}_{12}\text{O}_6$.

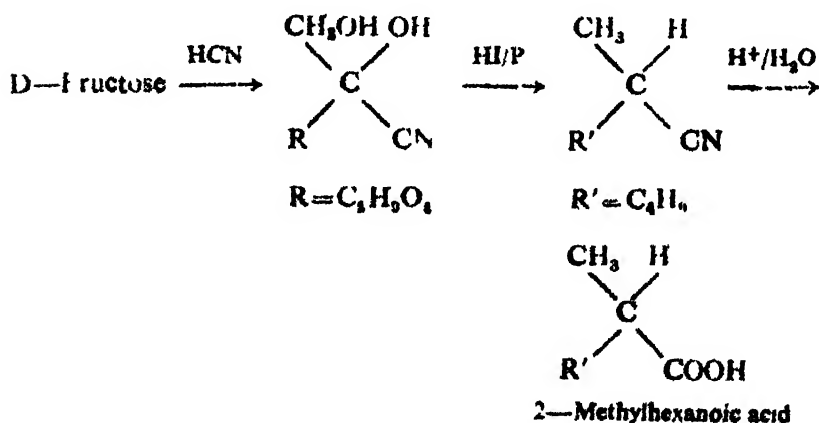
2. *Presence of a Straight Chain:* Fructose, on reduction, forms a mixture of polyhydric alcohols namely sorbitol and mannitol. Subsequent reduction of alcohols with HI/P yields 2-iodohexane. This shows that the carbon atoms are arranged in a straight line.

3. *Presence of an a keto group:* Several chemical reactions indicate the presence of a keto group.

a. It adds on HCN and H_2NOH .

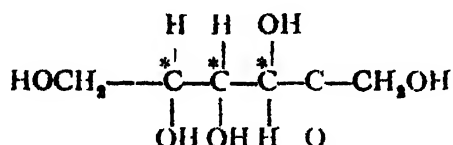
b. On oxidation with Br_2 water or nitric acid fructose gives a mixture of carboxylic acids i.e., glycollic, and tartaric. Since each contains fewer carbon atoms than fructose, shows the presence of a keto group in the chain.

c. The cyanohydrin of fructose, on reduction with HI/P followed by hydrolysis forms 2-methylhexanoic acid

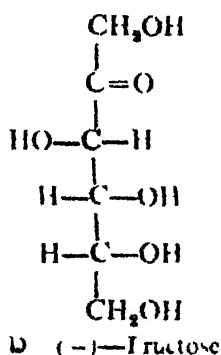


Since the carboxyl group in the resulting acid is present at the 2—position, therefore, the carbonyl group lies adjacent to a terminal carbon atom. The nature of the remaining carbon atoms is established by treating fructose with acetic anhydride.

4. With acetic anhydride, fructose forms a pentaacetyl derivative. Thus, like glucose, each carbon atom carries one —OH group. Keeping the above facts in mind, the following linear structure can be formulated for fructose



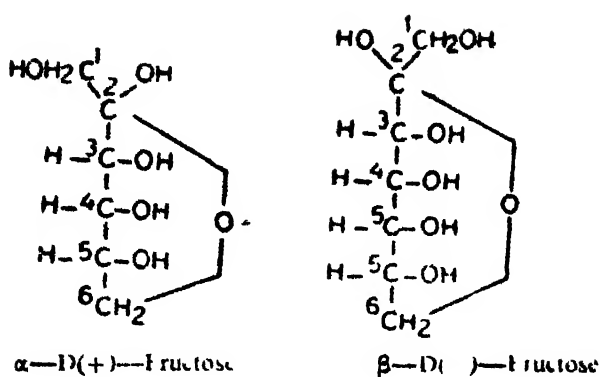
Fructose is an optically active compound; it contains three asymmetric carbon atom, therefore, it has $2^3 = 8$ stereoisomers. The natural sugar is D-(—)-fructose and has the following structure.



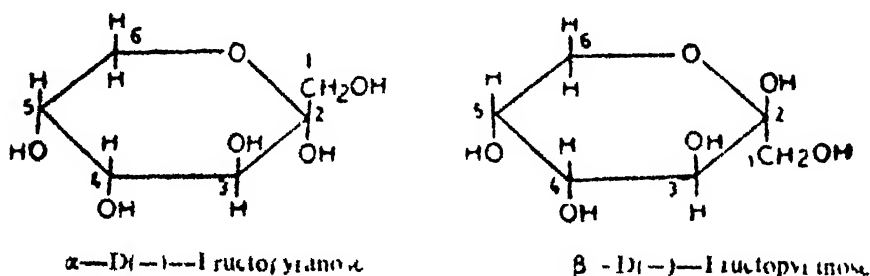
The open-chain structure of fructose is similar to glucose and is useful for understanding many aspects of carbohydrate chemistry but it leaves many questions still unanswered, for instance:

- It does not add on NaHSO_3 as ketones do
- It shows mutarotation.
- Like glucose, it forms two isomeric fructosides. Fructose displays the phenomenon of mutarotation, α -D-fructose $[\alpha] = +17^\circ$ and β -D-fructose $[\alpha] = -140^\circ$, when either the α — or the β — form is dissolved in water an equilibrium optical rotation of $[\alpha] = -93^\circ$ is obtained.

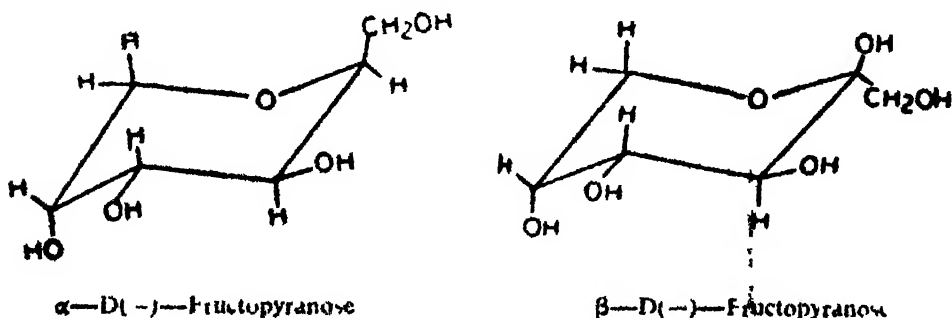
This has been accounted for on the basis of a ring structure for fructose.



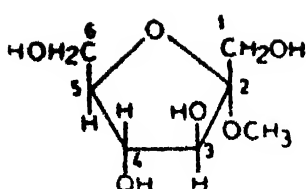
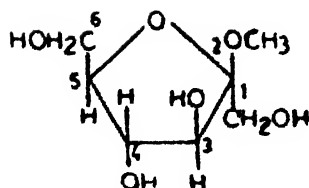
These two cyclic isomers differ only in the stereochemistry at C—2. D—Fructose forms two hemiketals: a six-membered pyranose form and a five-membered furanose form and each of these has α - and β -forms. These are represented below



Only one of these fructopyranose forms so far has been isolated and it has been assigned the β configuration. These structures may be drawn in their true chair forms as follows

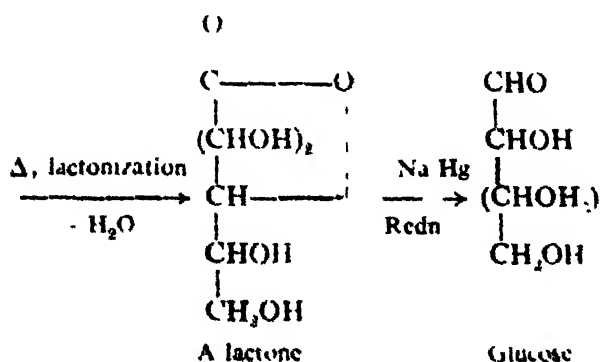
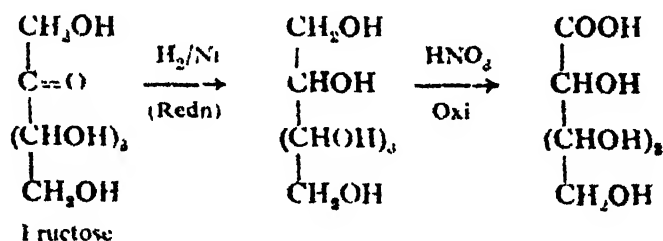
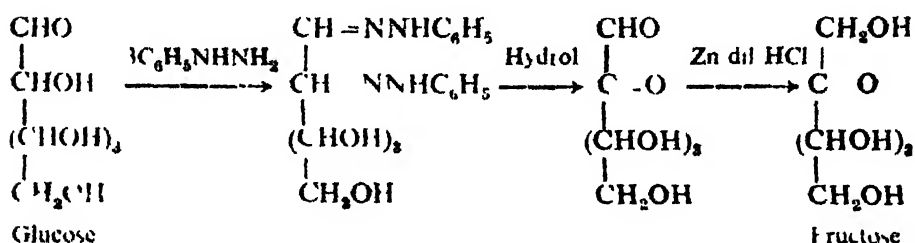


The fructofuranoses are unstable, except in the form of their glycosides, i.e., D—fructofuranose is present in cane-sugar and inulin. The fructofuranosides have the following cyclic structures:

Methyl-2- α -D-FructofuranosideMethyl-2- β -D-Fructofuranoside

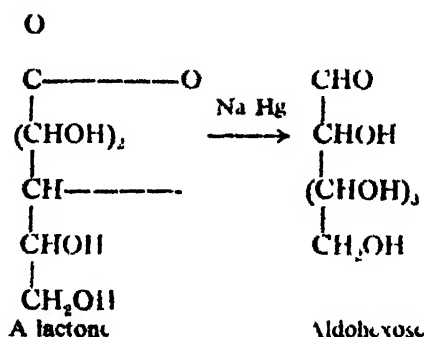
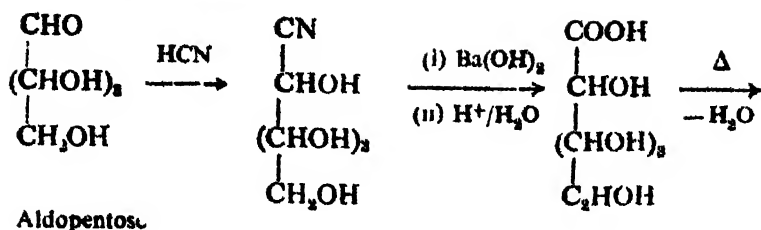
24.3.6 Conversion of Glucose into Fructose and vice versa

These conversions can be brought about by the following sequence of reactions.



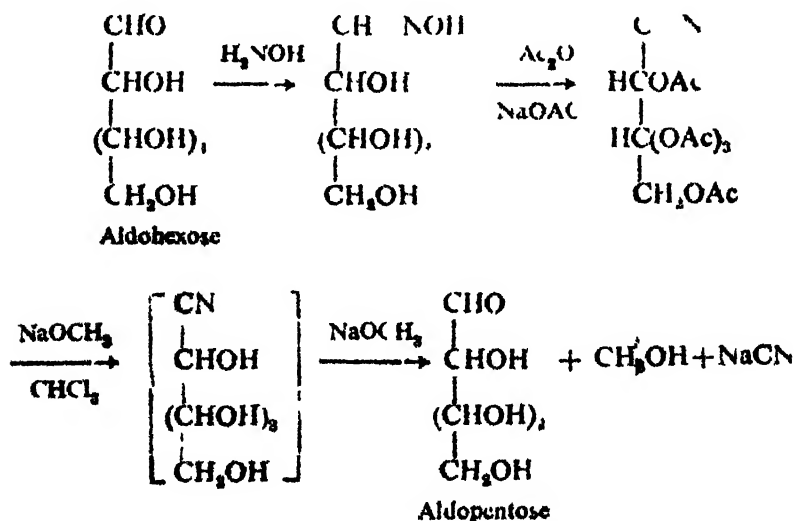
24.3.7 Ascending and Descending the Monosaccharide Series

The *Kiliani—Fischer reaction* enables us to convert an aldose into the next higher member. This chain-extension involves the addition of HCN to the aldehyde group. It is then hydrolyzed to aldonic acid. This is followed by lactonization and reduction with Na/Hg.



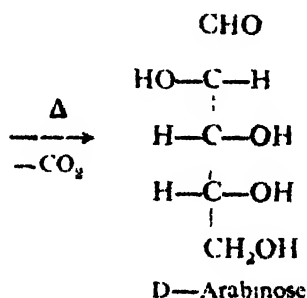
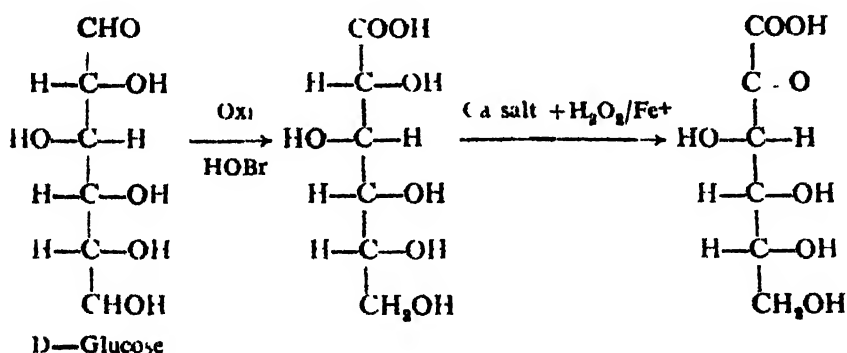
This step can be employed to extend the chain upto ten carbon atoms.

The reverse conversion, i.e., shortening of the chain can be accomplished by a process known as the *Wohl's degradation*. The aldose is first converted into the aldoxime, which on treatment with acetic anhydride is converted into the acetylated aldonitrile. The ester groups are removed under basic conditions and the cyano group is decomposed to the corresponding aldehyde.



A second procedure called *Ruff's Method* may also be employed for descending a chain of monosaccharides. The aldose is first hydrolyzed to

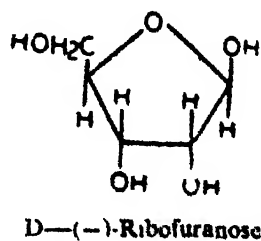
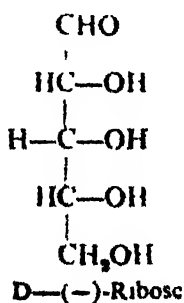
an aldonic acid and the calcium salt is then treated with *Fenton's reagent* (hydrogen peroxide and ferrous acetate). Water and carbon dioxide are eliminated and a lower aldose is obtained.



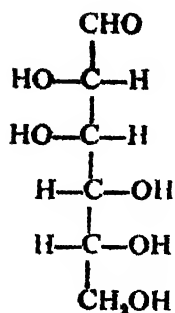
24.3.8 Other Important Monosaccharides

Several additional important monosaccharides are the following:

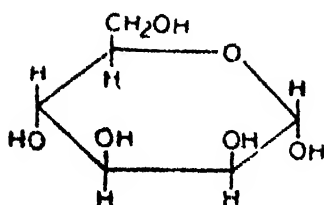
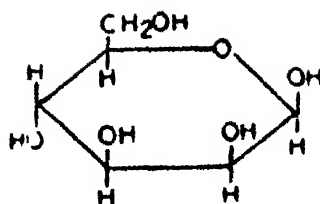
D-Ribose: Its hemiacetal form is related to a furan ring thus it is called a furanose.



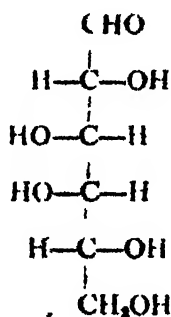
D-Mannose: Mannose occurs in the seed case of ivory nut and in the grains of barley and wheat. It is a crystalline substance and has a sweet taste. It is an optical isomer of glucose and differs from it in its configuration at C-2. Therefore, glucose and mannose are epimers. Mannose forms the same osazone as glucose. On reduction D-mannose forms mannitol.



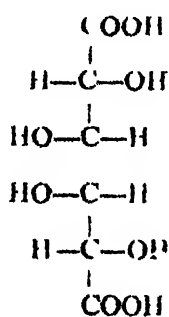
D-(+)-Mannose

 α D-(+) Mannose β D-(+)-Mannose

D-Galactose: Like D-Mannose it is also an optical isomer of glucose. Galactose and glucose differ in their configuration at C-4. It occurs in nature in the form of polysaccharides, i.e., milk sugar. It is a crystalline substance and on oxidation yields mucic acid.



D-(+)-Galactose



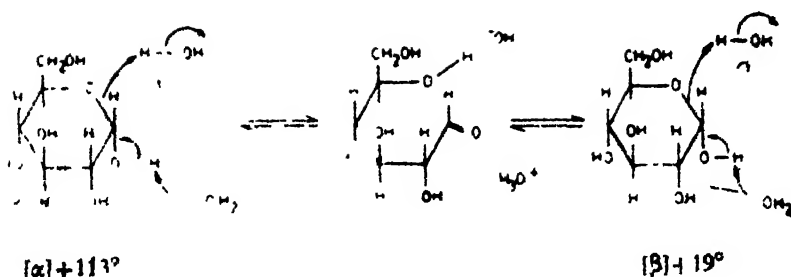
Mucic acid

24.4 MUTAROTATION

Glucose exists in two stereoisomeric forms namely the α - and the β -forms. Pure α -form (crystallized from methanol) when dissolved in water has a specific rotation of $+113^\circ$. The β -isomer (crystallized from acetic acid) on dissolution in water shows a rotation of $+19^\circ$. But over a period of time both give an equilibrium value of 52.5° . The phenomenon of change in specific rotation is called *mutarotation*. To account for this observation a cyclic structure was proposed for glucose in which the open-chain structure forms two anomeric hemiacetals (see p. 675) with the $-\text{OH}$ group present at C-5. Either of the forms establishes an equilibrium composed of 36.4% of the α - and 63.6% of the β -form of glucose. The aldehydic open-chain form of glucose is present in very small (0.1%) at any time.

Mutarotation is catalyzed by water.

Mechanistically it is a concerted process and involves the removal of a proton from the acetal hydroxyl and donation of a proton to the ethereal oxygen atom. This is shown below.



Mutarotation is catalyzed by a solvent possessing both acid and basic properties such as hydroxypyridine.

24.5 DISACCHARIDES

A disaccharide is made of two monosaccharides linked by a glycoside bond formed from the OH group of one monosaccharide to the anomeric carbon of the other.

This is also referred to as the β -linkage (see diagram on p. 682). The units can also be linked by an α -glycoside linkage (see diagram on p. 682).

The most important disaccharides of interest are sucrose, lactose, maltose and cellobiose. Only the first three occur free in nature. Disaccharides are also classified into two types, i.e., reducing and non-reducing.

24.5.1 Sucrose (Non-reducing)

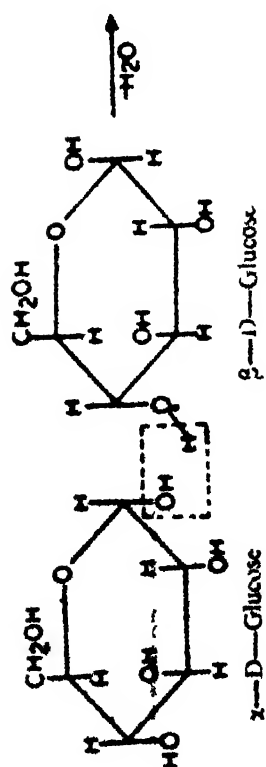
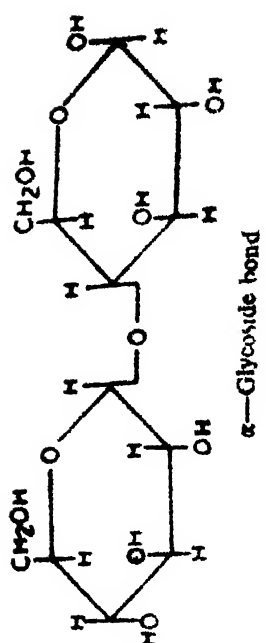
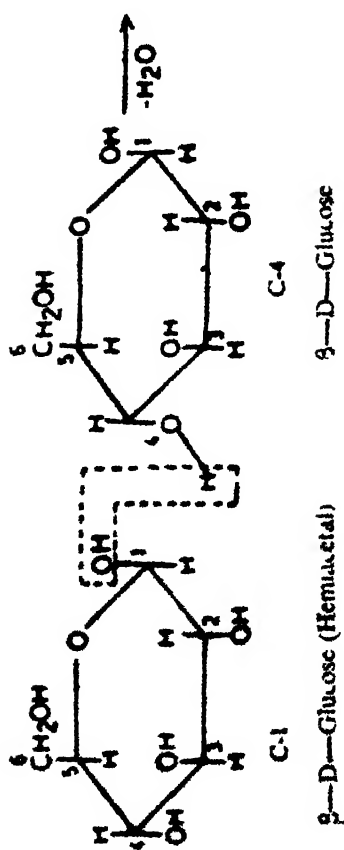
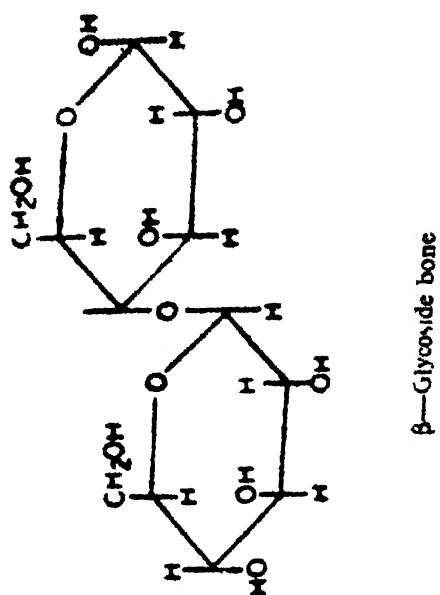
Sucrose is commercially the most important of the disaccharides. It is the sugar used by millions every day to sweeten food. It is obtained from sugar-cane which contains 15-20% of sucrose. An alternative source is sugar beets which contains 10-17% of sucrose.

Manufacture

For sugar manufacture, fresh sugar-cane stems are crushed in crushers to obtain a juice which is usually opaque and dark in color. The *begasse* is dried and employed as fuel. The juice is purified either by using milk of lime followed by treatment with sulfur dioxide (sulfonation) or with carbon dioxide (carbonation). It is then filtered to remove the suspended impurities. The juice may be filtered through activated charcoal to obtain a colorless product. The clear filtrate is then concentrated by multiple effect evaporators. The syrup so obtained is then boiled in vacuum pans till formation of sugar crystals commences. The sugar crystals along with the mother liquor (molasses) are centrifuged to separate the crystals. These crystals are usually sprayed with cold water to remove the last traces of molasses.

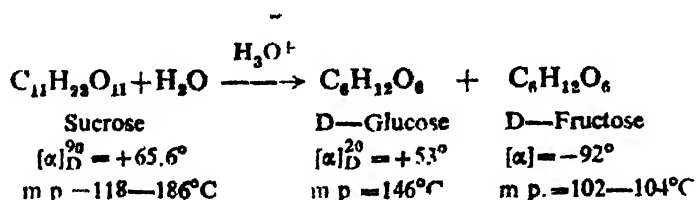
Properties

Sucrose is a colorless crystalline substance, highly soluble in water, but insoluble in most organic solvents. It contains one unit each of glucose and

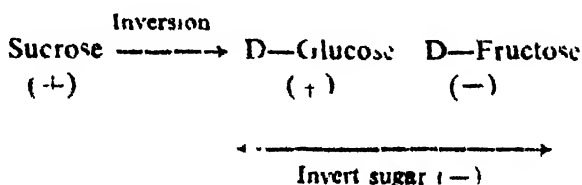


fructose which are reducing while sucrose itself is non-reducing because both anomeric carbons are linked in the acetal form. sucrose does not mutarotate or forms an osazone. These facts rule out the presence of a hemiacetal function. It also does not possess properties typical of monosaccharides, i.e., it does not reduce Fehling solution and does not form an osazone.

1. **Hydrolysis:** The optical rotatory properties of sucrose and its hydrolysis products are of interest. Hot dil acids hydrolyze sucrose to a mixture of equal amounts of D—glucose and D—fructose. The rotation of (+)-sucrose is $+65^\circ$. Since D—Fructose (-92°) rotates the plane of polarized

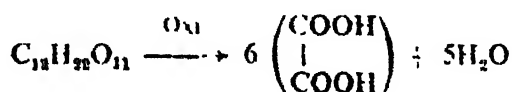


light to the left (—) to a greater extent than D—glucose ($+53^\circ$) does to the right (+), the mixture of sugar produced is slightly *laevorotatory*. The original sucrose, however, was *dextrorotatory*. Thus during hydrolysis the optical rotation of the solution has undergone an inversion or change in optical rotation from *dextro* to *laevo*. The mixture of sugar produced is known as *invert sugar*. This is summarized as follows:

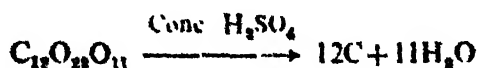


This mixture of sugars occurs extensively in honey.

2. **Oxidation:** Conc nitric acid oxidizes sucrose to oxalic acid.



3. **Dehydration:** In the presence of conc. sulfuric acid sucrose loses water to yield black carbon.



4. With conc. hydrochloric acid sucrose decomposes to laevulinic acid



5. *Fermentation.* An aqueous solution of sucrose in the presence of yeast yields alcohol on fermentation



6 *Esterification* The eight hydroxyl groups of sucrose can be esterified with acetic anhydride. The resulting compound is insoluble in water and has a bitter taste

7. *Non-ionic Detergents* Esterification of only one hydroxyl group with a long-chain fatty acid serves to make sucrose a non-ionic detergent. This detergent is bio-degradable

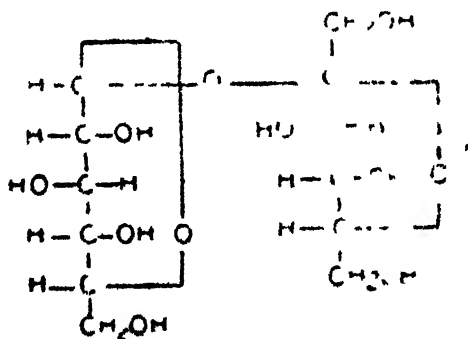
24.5.2 Constitution of Sucrose

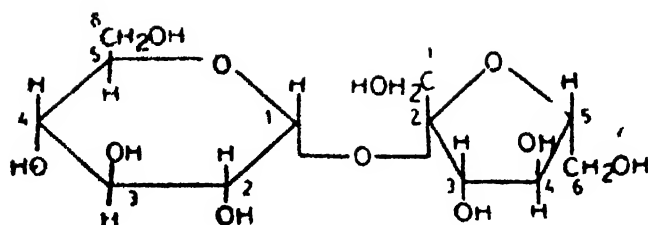
The structure of sucrose has been deduced from the following information

1. The molecular formula of sucrose has been found to be $\text{C}_{12}\text{H}_{22}\text{O}_{11}$

2 Hydrolysis of sucrose yields equal amounts of glucose and fructose. This shows that these two units are linked together through an oxygen atom. Sucrose is a non-reducing sugar, the two units are thus joined in such a manner as to destroy the possibility of forming a free aldehyde or keto group

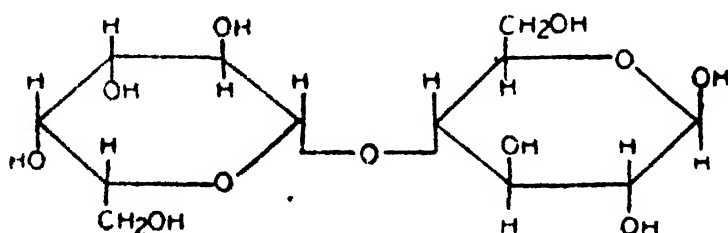
3 Esterification with acetic anhydride shows the presence of eight hydroxyl groups. Sucrose consists of one molecule of α -D-glucose and one molecule of β -D-fructose linked by the two glycosidic hydroxyl groups at C_1 of glucose and C_2 of fructose molecules. Its structure is shown below in both the methods of representation



 α -D-Glucopyranose β -D -Fructofuranose

Sucrose is thus an α -D-glucopyranosyl- β -D-fructofuranoside

24.5.3 Lactose (reducing)



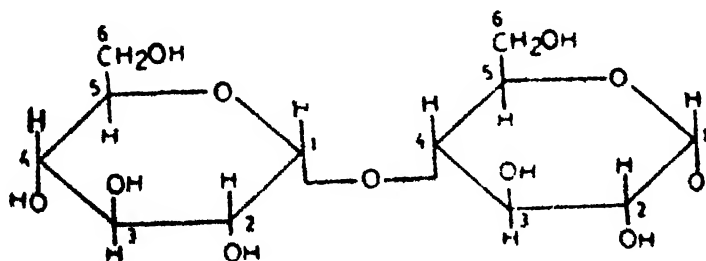
D-Galactose

D-Glucose

 β -(+)-Lactose

Lactose occurs in the milk of virtually all mammals to the extent of about 5 per cent. It is formed from D-galactose and D-glucose and the glycosidic hydroxyl group at C_1 of D-galactose is linked with the alcoholic hydroxyl group at C_4 of D-glucose. Lactose is, therefore, 4- β -D-galactopyranosyl D-glucopyranose. It reduces Fehling's solution and forms an osazone. Oxidation with bromine water leads to a carboxylic acid which is hydrolyzed to galactose and gluconic acid. Therefore, the reducing group is present in the glucose unit of lactose.

24.5.4 Maltose (reducing)



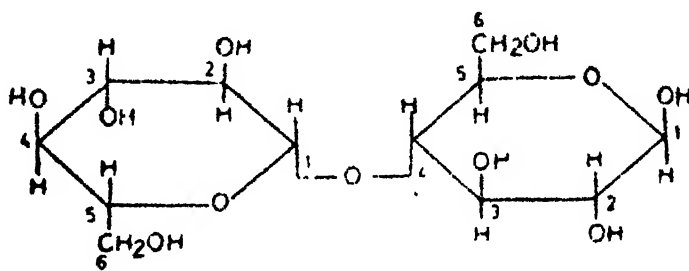
D-Glucose

D-Glucose

 α -(+)-Maltose

Maltose is obtained by the partial enzymatic hydrolysis of starch by the enzyme diastase. It occurs as an intermediate in the preparation of ethanol by the fermentation process. First starch is hydrolyzed by the enzyme diastase to maltose which is hydrolyzed in turn to D-glucose by the enzyme maltase. Glucose is then fermented by means of yeast to give ethanol and carbon dioxide. Maltose consists of two D-glucose units. The oxygen bridge in maltose joins the C_1 of one unit with C_4 atom of the second unit. Consequently, the glycosidic 1-hydroxyl group of the second molecule of glucose is free. It is thus 4-(α -D-glucopyranosyl)-D-glucopyranose. Maltose reduces Fehling solution. On oxidation with bromine water it is converted to a monocarboxylic acid, i.e., maltobionic acid ($C_{12}H_{22}O_{11}COOH$).

24.5.5 Cellobiose (reducing)



8 (+)-cellobiose

It is obtained by the acid catalyzed hydrolysis of cellulose (cotton fibres) followed by alkaline hydrolysis of the octaacetate formed. It is similar to maltose in its properties, except that it is not affected by the enzyme maltase. It consists of two D-glucose units joined at the $C-1$ and $C-4$ hydroxyl groups. To represent appropriate attachment of a β -linkage to $C-4$, it is necessary to flip one β -glucose unit through 180° .

24.6 POLYSACCHARIDES

Polysaccharides are natural polymers. These are high molecular weight molecules made up of monosaccharide (D-glucose) linked together through oxygen atoms to form chain of varying lengths. The monosaccharide units are linked by glycoside linkage. As a class they occur widely in plants and animals; and some serve as reserve for food supplies. Two of the important polysaccharides are starch and cellulose both of which can be represented by the general formula $(C_6H_{10}O_5)_n$. Polysaccharides do not exhibit the characteristic reactions of the aldehyde group.

24.6.1 Cellulose

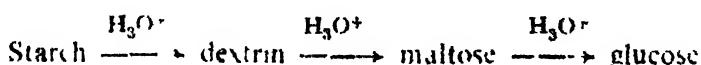
Cellulose is widely distributed in plants and is the chief constituent of the cell walls of plants and a main constituent of cotton, wood, corn cobs,

paper, straw and many other substances. Leaves have about 10% cellulose, wood has about 50%, cotton 90% and filter paper consists almost entirely of cellulose. It yields glucose on hydrolysis. Partial hydrolysis, however, yields the disaccharide, cellobiose; thus cellobiose is the structural unit of the cellulose polymer.

The molecule has a linear chain and the structure is shown on the next page. Cellulose is a colorless solid. Although it contains so many hydroxyl groups it is insoluble in water. This is attributed to the fact that its linear closely packed structure is formed through hydrogen-bonding which makes interaction with water difficult. The human digestive tract breaks down starch to glucose, but it does not contain the necessary enzymes to hydrolyze the β -glucose linkages and thus cellulose is not used as a food material. Various derivatives of cellulose namely cellulose nitrate and cellulose acetate find many commercial uses.

24.6.2 Starch

Starch is a polymer of glucose and occurs naturally as granules in the roots, tubers and stems of various plants. It comprises a large percentage of potatoes, cereals, rice, and barley. Starch constitutes the main carbohydrate reserve of plants. The animal starch is called *glycogen*. Partial hydrolysis of starch yields maltose while complete hydrolysis either enzymatically or chemically forms D-glucose. The hydrolysis takes place through dextrin (the polysaccharides of intermediate chain length that are formed from starch components by the action



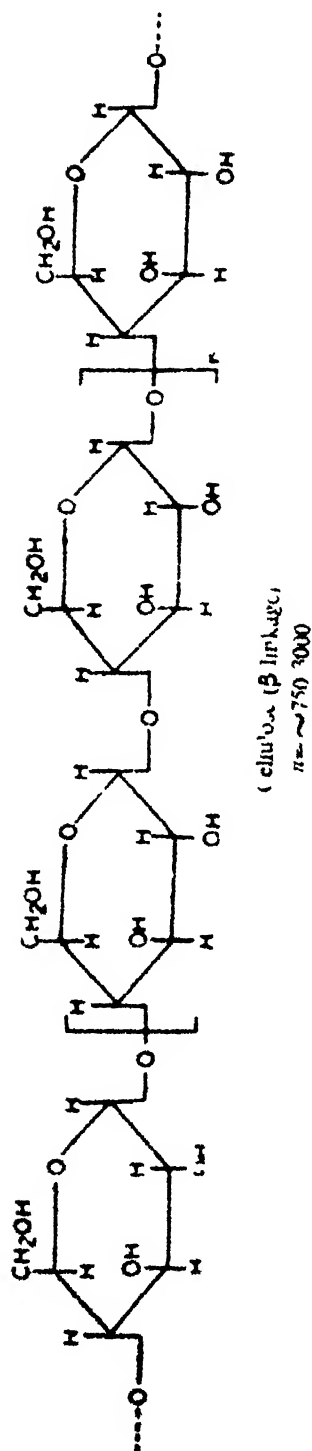
of amylases are called dextrans). Starch is not a single substance but consists of two main types of polysaccharides, *amylose* and *amylopectin*. These two portions can be separated by fractionating starch with hot water.

Amylose constitutes 20% of starch and is sparingly soluble in hot water. It consists of unbranched chains, and the glucose molecules are linked by α -glucosidic linkage at C-1 and C-4 atoms (p. 690).

Amylose is responsible for the blue color of the starch iodine test.

Amylopectin: Starch granules comprise about 13% of amylopectin. It is a highly branched molecule and has an average molecular weight of over one million. A partial structure is given on page 692.

Because of its branched structure, starch is not suitable for plastics and fibres like cellulose. It is, however, useful as food because animals have the enzymes necessary to break the α -glucoside linkages.



24.6.3 Other Important Polysaccharides

Glycogen: Starch is a major nutrient for animals. It is converted to (+)-glucose by animal metabolism. Glucose is repolymerized to form glycogen in the liver. It serves as a reserve energy source. Glycogen consists of branched chain of glucose molecules.

Inulin: It is another reserve carbohydrate of plants. It occurs in dahlia bulbs and in Jerusalem artichokes.

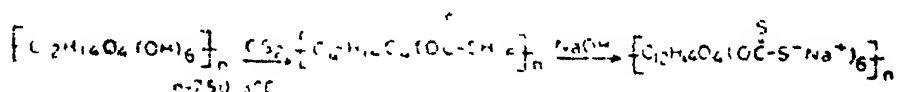
Chitin: It is the structural material of lobster shells, insects and fungi. On heating with dil. hydrochloric acid, chitin breaks down to D—glucosamine and acetic acid.

Agar: It is obtained from seaweed. It is used in biological laboratories to grow columns of bacteria.

24.7 ARTIFICIAL SILK

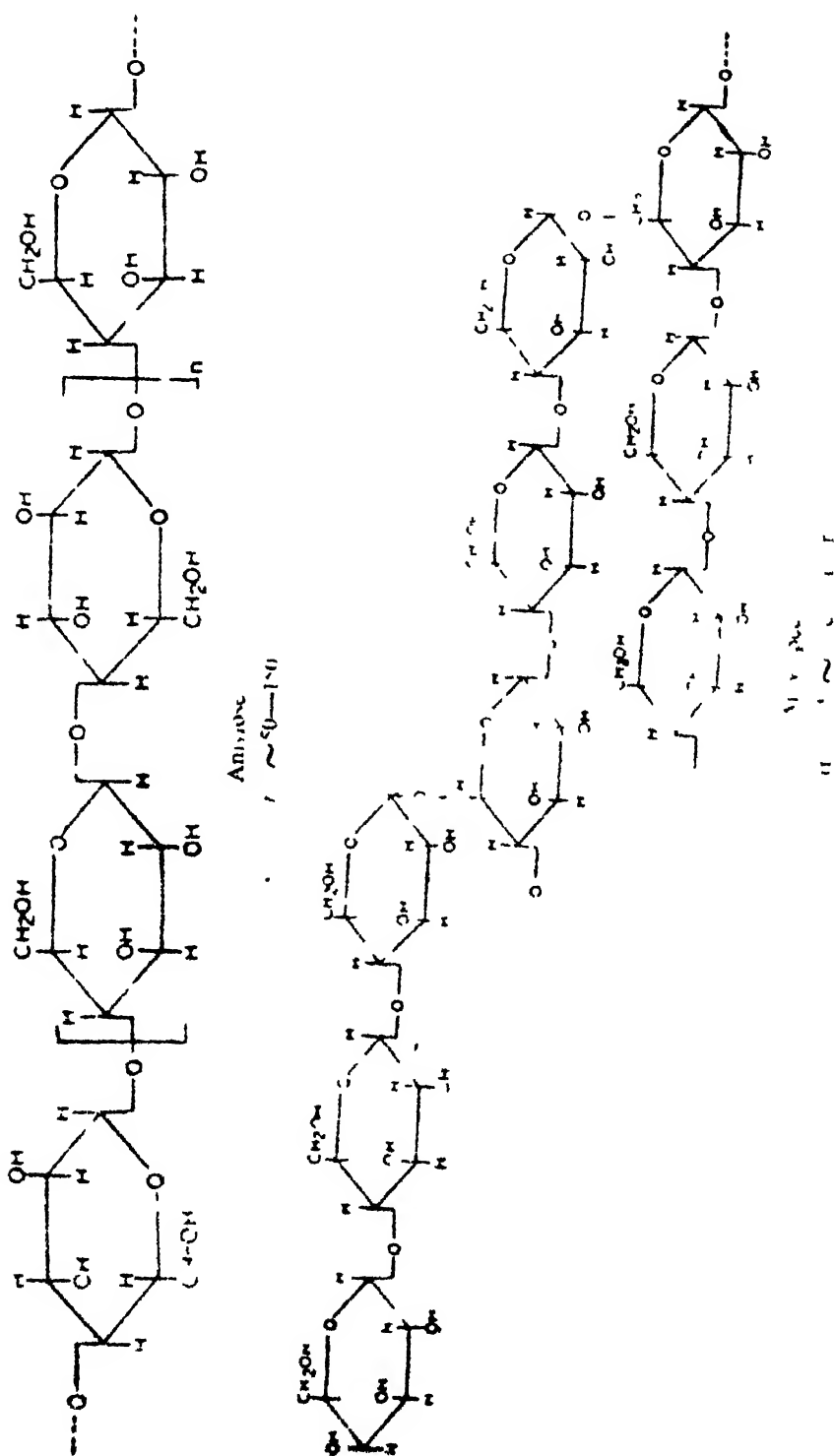
Natural silk is obtained as a secretion from the silk worm in the form of a filament. This type of silk is a protein material and contains nitrogen. Artificial silk (rayon) does not contain nitrogen. Very important commercial products are obtained from cellulose first by dissolving it and then precipitating it from the solution. This is accomplished by two methods namely the *viscose* or the *xanthate process*, and *acetate process*.

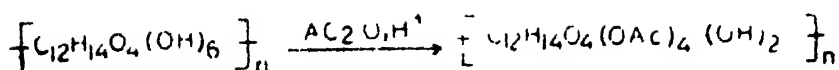
Viscose Process: Cellulose is separated from wood pulp with the help of alkali. This is allowed to age during which time the molecular weight is reduced due to degradation. Then carbon disulfide is mixed with the pulp to convert cellulose into sodium salt of cellulose xanthate. A viscous solution is thus obtained and is called viscose.



This is again allowed to age and then drawn into filaments by passing through a bath containing dil. sulfuric acid, sod. bisulfate and zinc sulfate. The xanthate is hydrolyzed back to cellulose. The fibre so obtained is called *viscose rayon* and is used in text. s.

Acetate Process: Cellulose esters are more important nowadays. In this case, the cellulose is treated with acetic anhydride and a catalytic amount of a mineral acid, to obtain varying degrees of cellulose acetate. The desired degree of substitution is obtained by reacting the fully acetylated product with water.

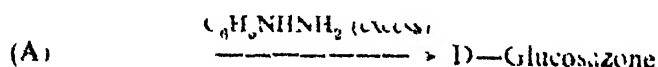
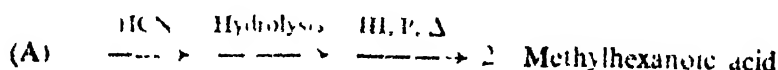




A mild hydrolysis yields a completely acetylated cellulose called *triacetate*. A further hydrolysis yields a product soluble in acetone and is called a *secondary acetate*. Both these products are used in making fibres.

QUESTIONS

- 24.1 Describe each of the following with a suitable example: Mutarotation, a glycoside, Fehling test, pyranose, hemiacetal, amylose, and anomers.
- 24.2 Define each of the following and give a specific example and write the structural formula: A ketose, pentose, osazone, disaccharide and hexose.
- 24.3 Explain by writing a formula, what is meant by the term D—sugar
- 24.4 What is invert sugar and why is it so named?
- 24.5 How would you establish that the reducing part in lactose is the glucose molecule?
- 24.6 Explain why, although cellulose contains so many -OH groups, it is insoluble in water.
- 24.7 Draw the most favorable chair form for α -D—glucopyranose.
- 24.8 Compound A, $\text{C}_6\text{H}_{12}\text{O}_6$, reduces Fehling solution and is optically active. It also responds to the following reactions:



Suggest a structure for A.

- 24.9 Explain why maltose and lactose are reducing but sucrose is non-reducing. Use the structural formulas.
- 24.10 (a) Write the general structure of the cellulose molecule.
(b) What is the main difference between cellulose and amylose?
(c) Why is starch but not cellulose digestible by humans?
- 24.12 Name a polysaccharide that gives only glucose when completely hydrolyzed.
- 24.13 What are carbohydrates and how are they classified? How does sucrose occur in nature? Give one method for its large scale preparation. How is it related to glucose? What tests would you perform to distinguish it from glucose and fructose?

- 24.14 How is fructose prepared? Establish its structure. How is it converted into glucose?
- 24.15 Write an account of the methods for the conversion of an aldose to a ketose and *vice versa*.
- 24.16 (a) What are carbohydrates? What are their importances? How is glucose related to cellulose?
(b) Discuss briefly the structure of glucose.
- 24.17 (a) What are carbohydrates and how are they classified?
(b) Show the series of reactions one would use to convert;
(i) aldohexose into aldopentose and *vice versa*
(ii) glucose into fructose and *vice versa*.
- 24.18 Describe the evidence which indicates a cyclic structure for fructose.
- 24.19 (a) Give in brief the reasons how the open-chain structure of glucose was found unsatisfactory?
(b) How will you prove by using a classical method that the fructose component in sucrose has the furanose form?
(c) Mention two methods for methylation of sugars, stating their advantages and limitations.
- 24.20 (a) Outline the various steps in the manufacture of cane-sugar from sugar-cane.
(b) How can the following conversions be carried out?
(i) a pentose into a hexose
(ii) an aldohexose to a ketohexose
- 24.21 Why is mutarotation catalyzed by hydroxypyridine but not by pyridine alone?

Alkaloids

The term *alkaloid* is not an easy term to define with precision but it may be said to include all basic nitrogenous compounds which occur in plants and possess physiological properties. Because of their physiological properties, many alkaloids form an important group of organic medicinal chemicals. The first alkaloid was discovered by the German pharmacist Serturner (1805) who isolated morphine from opium. He subsequently described it as a basic, salt forming substance having the principal physiological action of the drug. The discovery of morphine was quickly followed by the isolation of other alkaloids chiefly by Pelletier. The first volatile alkaloid, coniine was isolated in 1827 and nicotine in 1828. A large number of chemicals resembling alkaloids, but not found in plants, have been prepared in the laboratory and closely resemble many of the naturally occurring alkaloids in constitution and physiological action. Naturally they occur in nearly all parts of plants, but particularly in seeds, roots, leaves and barks. Alkaloids are basic in nature and the nitrogen atom is often a part of the heterocyclic ring system. Chemically complex though alkaloids are, their study is aided by the fact that they are either crystalline or form salts which crystallize well and can be separated by standard methods. Alkaloids are also optically active and form precipitates with many reagents, some of which are given below:

Auric Chloride. Auric chloride combines with alkaloidal hydrochlorides to form well defined crystals of aurichlorides. These are sparingly soluble in water

Bismuth Potassium Iodide (Kraut's reagent): It forms a brick red color and is used to isolate simple water soluble bases

Iodine (Wagner's reagent): Iodine added to aqueous potassium iodide is the most useful reagent. In very dilute solutions a reddish—brown precipitate is formed, which in strong solution aggregates at once to a greenish—black mass.

Potassium Mercuric Iodide (Mayer's reagent). The reagent is prepared by adding KI to mercuric chloride until the mercuric iodide first precipitated redissolves. This is the best reagent for detecting alkaloids. In dilute solutions an opalescence is obtained, while in concentrated solution, a yellowish white flocculent precipitate is formed.

Picric Acid: Picric acid precipitates alkaloids as picrates from solutions of alkaloidal salts and these may often be crystallized.

Alkaloids are classified chemically according to the heterocyclic ring present in them, such as pyridine alkaloids, quinoline alkaloids, isoquinoline alkaloids, indole alkaloids, etc. Some alkaloids may be classified under more than one of the above groups or under additional groups. Atropine and cocaine contain both a pyrrolidine and a piperidine ring.

24.1 OCCURRENCE OF ALKALOIDS

Plants are the main sources of alkaloids. They occur in the leaves, seeds, roots and barks of a large variety of plants. The alkaloid content of plants varies with its locality and the climate. Closely related alkaloids often occur together in the same plant. Some plant sources of alkaloids are listed below.

Nicotine —occurs in tobacco plants (2-8 %)

Quinine —bark of cinchona tree

Conine —seeds of hemlock herb

Cocaine —in coca

Morphine —opium poppy

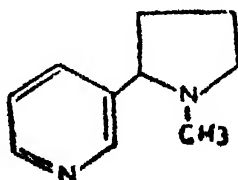
Piperine —in black pepper

25.2 NOMENCLATURE OF ALKALOIDS

Simple alkaloids such as conine, nicotine, etc., though they can be named according to the IUPAC system, are usually known by their trivial names. On the other hand, the complex alkaloids like morphine, cocaine, reserpine, etc., are known by their common names only. These names are based either on their physiological action or their chemical structure.

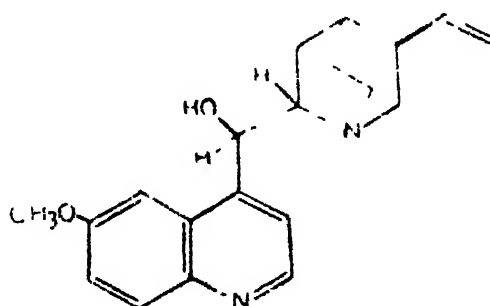
25.3 PHYSIOLOGICAL ACTION OF ALKALOIDS

Alkaloids are widely used as drugs and possess pronounced physiological properties.



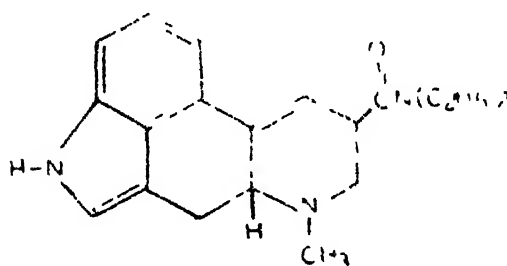
Nicotine (Pyridine ring)

It is highly poisonous and is used as an insecticide. It increases the heart beat and has no therapeutic value.



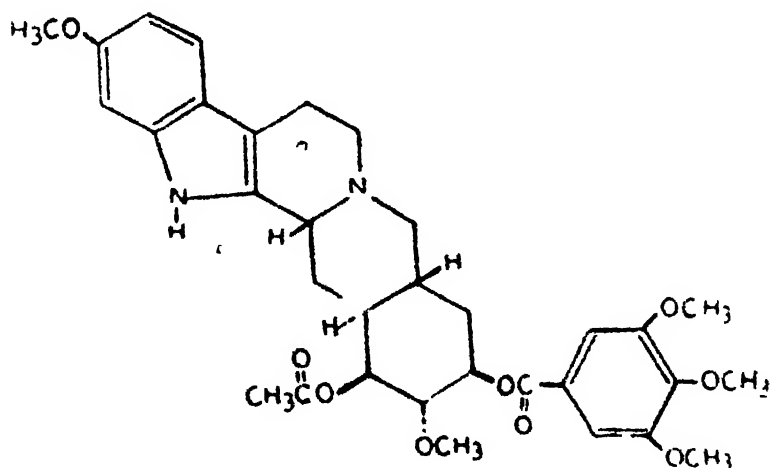
Quinine (Quinoline ring)

It is widely employed in the treatment of malaria.



Lysergic acid (Indole ring)

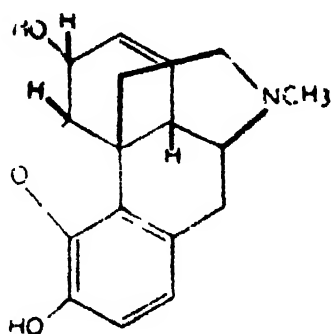
The ergot fungus produces the ergot alkaloids of which lysergic acid is the best known. The dimethylamide of this acid does not occur naturally and



Reserpin (Indole ring)

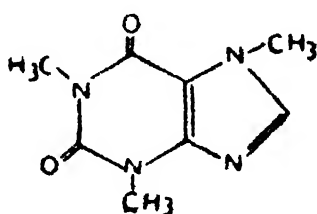
is known as LSD. It is hallucinogenic and causes a physiological state resembling schizophrenia. It is useful in the study of mental disorder.

Reserpine isolated from *Rauwolfia serpentina* which grows widely in the foothills of the Himalayas, has been used to treat snake bite, epilepsy, insanity and as a tranquilizer



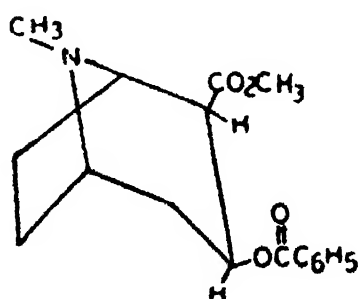
Morphine (Piperidine)

It is used as analgesic or pain killer and as a sedative. It has a depressant action on various parts of the nervous system



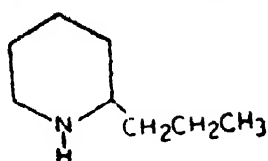
Caffeine (Pyrimidine and imidazole)

It is a heart stimulant and affects the central nervous system



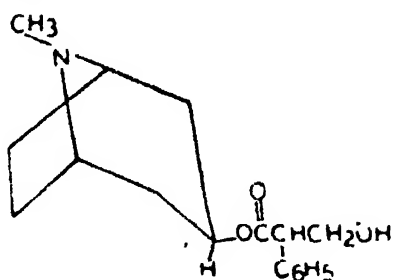
Cocaine (Tropane ring)

It is toxic and in small doses is used as a local anesthetic.



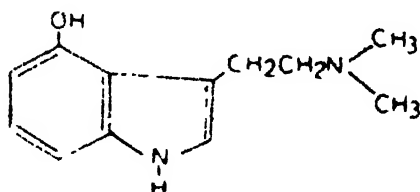
Coniine (Piperidine ring)

It is the active principle of water hemlock.



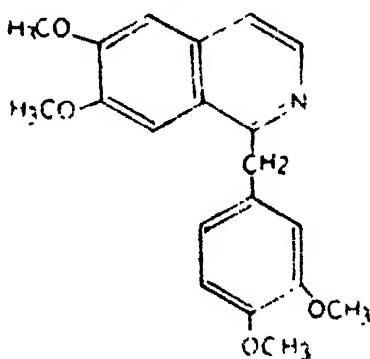
Atropine (Tropane ring)

In dilute solutions it is used in ophthalmic examination since it causes a dilation of the pupil.



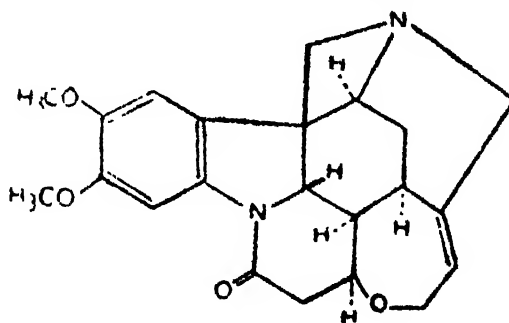
Pislocine (Indole ring)

It possesses hallucinogenic properties



Papaverine (Isoquinoline ring)

It is used as an antiplassmodic for smoothening muscles.



Brucine (Indole ring)

It is used for resolving racemic acids. It is toxic and produces painful convulsions.

25.4 ISOLATION AND STRUCTURE DETERMINATION OF ALKALOIDS

The pulverized plant material is extracted with an acid to isolate the alkaloid. The extract is treated with an alkali (caustic soda or ammonia) to release the free bases. Purification can then be effected by any of the general methods such as crystallization, distillation or chromatographic techniques. Sometimes alkaloids are precipitated from their solutions in the form of insoluble salts or complexes by reagents such as picric acid or mercury salts.

Alkaloids being chemically complex their structural assignment is accomplished by a careful examination of their chemical properties and spectroscopic examination. Some of the general methods are described below:

1. **Molecular Formula:** Elemental analysis and molecular weight determination are carried out to obtain the molecular formula.

2. **Functional Groups.** The nature of the functional group is established by performing individual tests for each group

- a. **Nitrogen Functional Groups:** Nitrogen may be present in one of several types of functional group.

Amino group: This may be confirmed by its reaction with acetic anhydride or benzoyl chloride.

Amide group: Products of hydrolysis, particularly evolution of ammonia gas indicates the presence of this functional group.

N--methyl group: Formation of methyl—, dimethyl—, or trimethyl—amine on distillation with KOH indicates an N-methyl grouping.

b. *Oxygen Functional Groups*: Oxygen atom may be present in the form of the following types of functional groups.

Hydroxyl: It can be detected by acetylation or benzylation as in the case of amino group.

Phenolic—OH: Solubility in KOH and a characteristic color with FeCl_3 solution indicates a phenolic—OH.

Alcoholic—OH: Dehydration takes place in this case with conc. sulfuric acid.

Carboxyl: This group is detected by its solubility in NaHCO_3 .

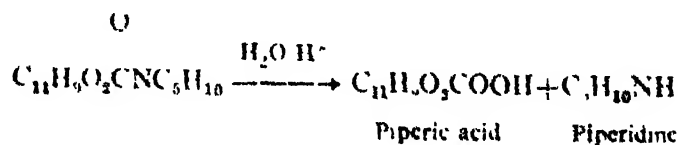
Ester: The hydrolysis products (acid+ alcohol) are identified.

Methoxyl: The presence and number of methoxyl groups is established by the *Zinck method*. According to this the alkaloid is heated with conc. HI. The methoxyl group is converted into CH_3I which is absorbed in alcoholic silver nitrate solution and AgI is precipitated. From the amount of AgI formed the number of methoxyl groups is established.

3. *Unsaturation*: Presence of unsaturation is detected either by bromination or catalytic hydrogenation. The latter method also determines the number of double bonds in the molecule.

4. *Degradation*. Alkaloids being complex molecules, they are broken chemically into simpler fragments. These units are then identified and the structure of the alkaloid formulated. Some of these techniques are the following:

a. *Hydrolysis*: An alkaloid containing an amide or ester function is split into two fragments, for instance:

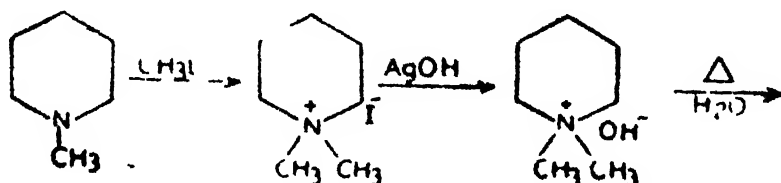


These hydrolysis products, after characterization, give a pretty good idea about the structure of an alkaloid.

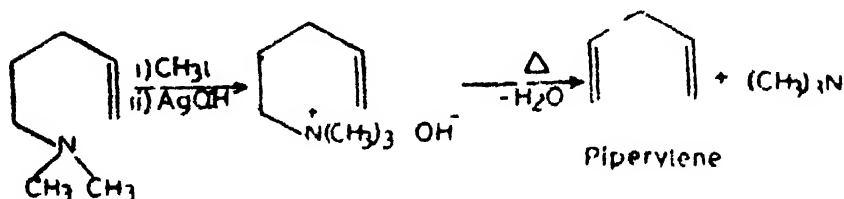
b. **Oxidation:** Depending on the oxidizing agent, a variety of products are obtained when an alkaloid is subjected to oxidation.

c. **Distillation with Zn Dust:** Dehydrogenation takes place according to this method and a basic skeleton of the alkaloid is obtained. Morphine, for example, yields the parent structure, phenanthrene, while ricinine gives pyridine.

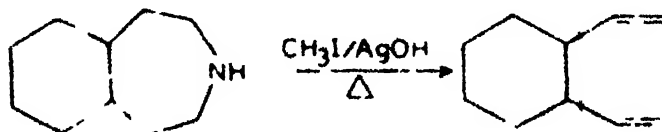
d. **Exhaustive Methylation:** A fair amount of information about the nature of the heterocyclic system is obtained from this method. The alkaloid is repeatedly treated with CH_3I and AgOH heated. The final product so obtained is free of nitrogen. This is illustrated by the following examples: N-methylpiperidine yields piperylene



N Methylpiperidine



Similarly, a diene is obtained in the following case



3. **Synthesis:** The structure is further examined on the basis of spectral analysis and confirmed by its synthesis starting from simple materials.

We will now examine the constitution of several alkaloids

25.5 NICOTINE

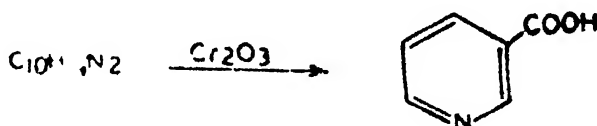
It is the principal alkaloid of tobacco leaves and occurs to the extent of 0.5—8%. The smoke of a cigarette can yield 6—8 mg of nicotine. Nicotine salts are used as insecticides.

Properties

1. It is one of the few natural liquid alkaloids. It is colorless, volatile and strongly alkaline.
2. On exposure to air it turns brown and acquires the odor of tobacco.
3. The natural alkaloid is *levo*—rotatory.
4. It has no therapeutic applications. It increases the heartbeat rate. Nicotine causes a discharge of epinephrine and this hormone raises blood pressure.

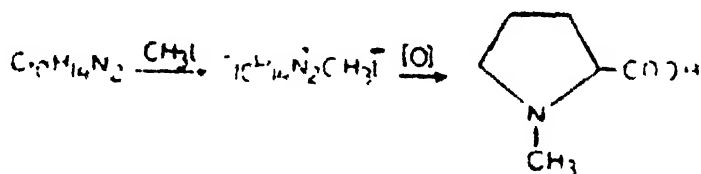
25.5.1 Constitution

1. The molecular formula of nicotine is, $C_{10}H_{14}N_2$.
2. It behaves like a tertiary amine because it does not give an acetyl derivative with acetic anhydride.
3. Nicotine, on oxidation with chromic acid, yields nicotinic acid (β —picolinic acid).



This suggests that a basic pyridine skeleton with a side-chain is present.

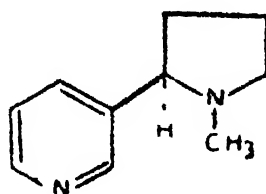
4. Treatment of nicotine with CH_3I forms a methiodide derivative, which on subsequent oxidation forms hygrinic acid (N—methylpyrrolidine α —carboxylic acid)



This suggests that a N—methylpyrrolidine ring is linked at the 3—position of pyridine.

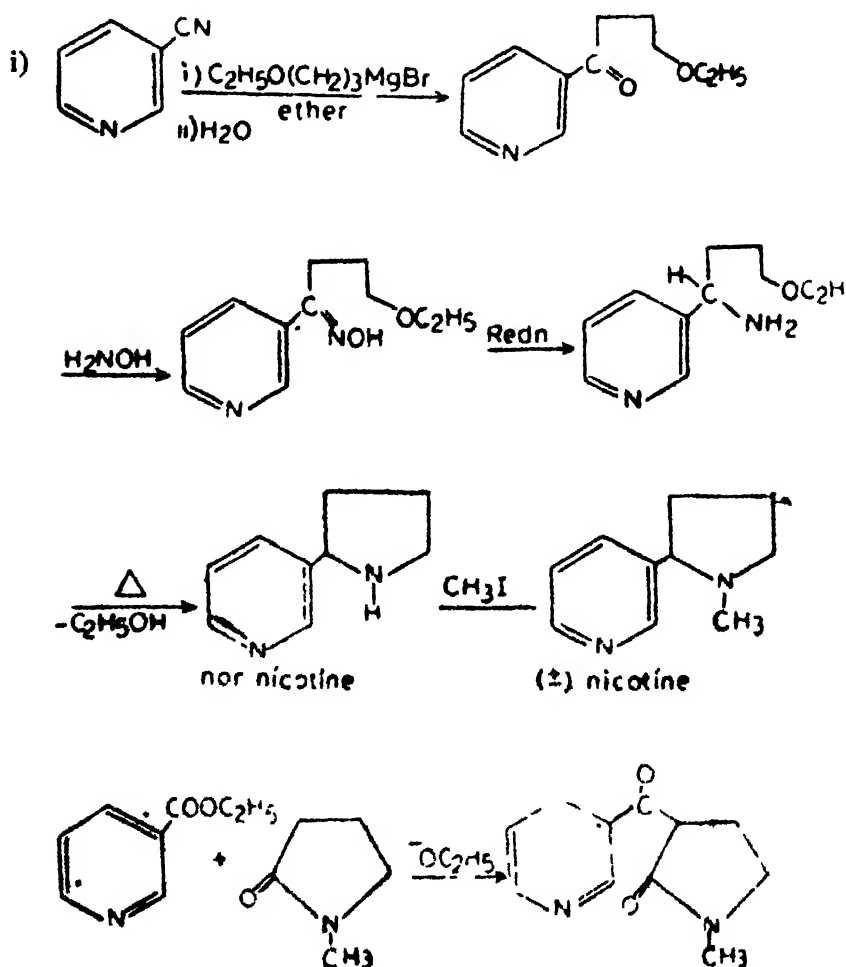
5. The position of the attachment of side chain is further established by bromination and hydrolysis of the bromo derivative with $Ba(OH)_2$. A mixture of three products, namely nicotinic acid, malonic acid and methylamine

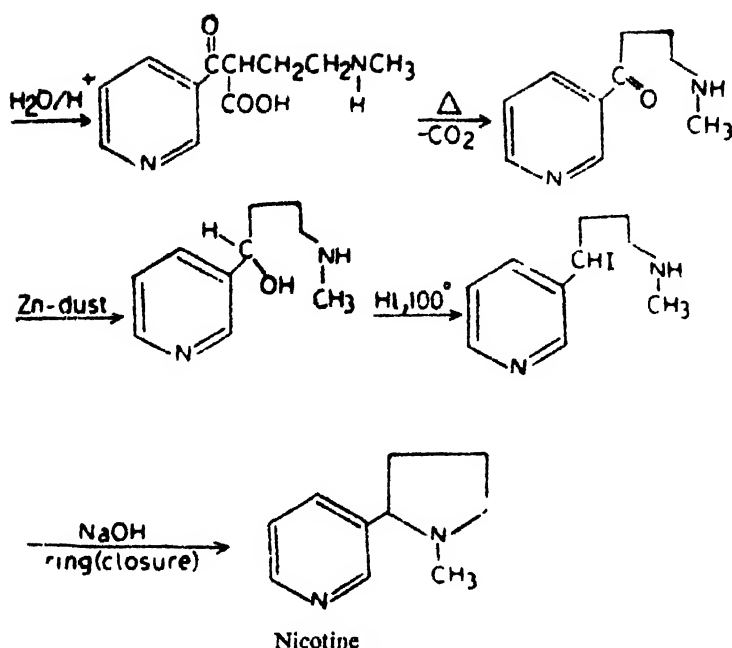
is formed. The formation of these three fragments suggests that the attachment is at position—3. Nicotine is thus a combination of pyridine and N—methylpyrrolidine as follows.



Nicotine

6. This structure has been confirmed by an independent syntheses of nicotine.





25.6 CONIINE

It is the poisonous principle of the hemlock herb and the first plant alkaloid to be synthesized. Coniine is of classical interest because this was the poison used in the execution of the Greek philosopher Socrates in 399 B.C.

Properties

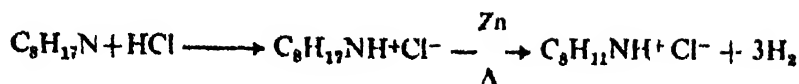
1. It is a colorless oily liquid, soluble in water and strongly alkaline.
2. It turns brown on exposure to air.
3. It is optically active and dextro rotatory $[\alpha] +15.7^\circ$.

25.6.1 Constitution

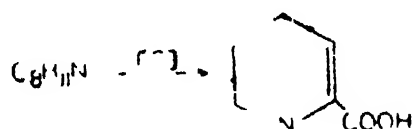
1. Its molecular formula is $\text{C}_8\text{H}_{17}\text{N}$.
2. Its reaction with acetyl chloride shows that it is a secondary amine.



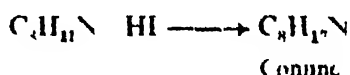
3. The key step in the determination of its structure was zinc—dust dehydrogenation. Coniine forms a salt with hydrochloric acid, the hydrochloride, on zinc—dust distillation yields a base which is short of six hydrogen atoms from the parent compound.



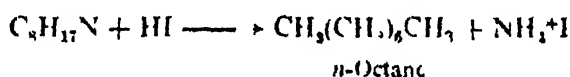
This base, on oxidation, forms α -picolinic acid. The oxidation reaction



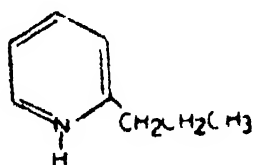
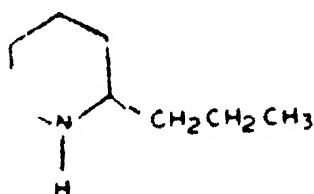
suggests that two carbon atoms have been lost; therefore, the original base must have a propyl chain attached at the 2-position of the pyridine ring. Reduction of this compound with conc. HI regenerates conine, and reduc-



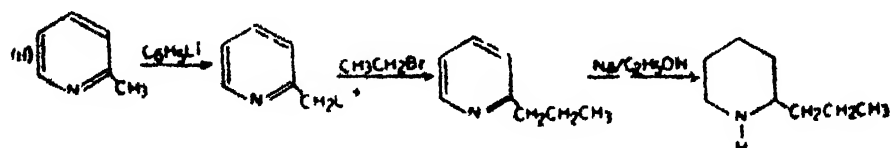
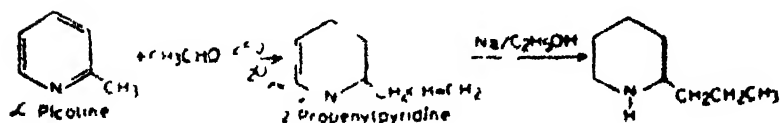
tion of conine with HI provides ammonia and *n*-octane. The propyl radical,



therefore, is *n*-propyl rather than *iso* propyl. Conine is thus 2-propylpiperidine and the base is 2-propylpyridine, also called convrine.



5. This structure was confirmed by its syntheses



25.7 PIPERINE

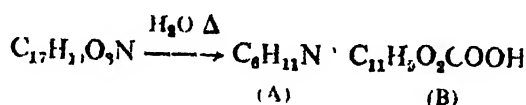
It occurs in black pepper (*Piper nigrum*) and has been used as a flavoring agent in brandy and as an insecticide for house-flies

Properties

1. It is sparingly soluble in water
2. It is relatively less toxic than many other alkaloids.
3. It is optically inactive but is capable of exhibiting *cis-trans* isomerism.

25.7.1 Constitution

1. The molecular formula of piperine is $C_{17}H_{19}O_3N$
2. On hydrolysis it degrades into piperidine (A) and piperic acid (B).

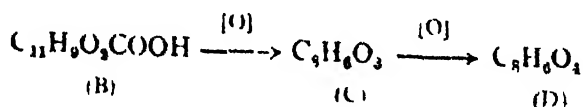


This suggests that piperine is the piperidinamide of piperic acid.

The structure of fragment (B) has been established as follows:

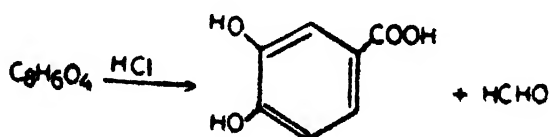
(i) Chemical tests show that it contains one carbonyl group and two double bonds

(ii) On oxidation with $KMnO_4$ (B) forms piperonal (C) and subsequently piperonylic acid (D)

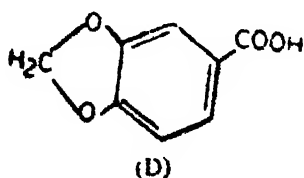


The acid (D) has 4C and 4H less than piperic acid (B).

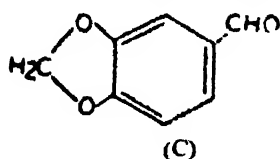
(iii) On heating with conc. HCl at 200° , piperonylic acid (D) forms proto-catechuic acid i.e., 3, 4-dihydroxybenzoic acid and formaldehyde. Since



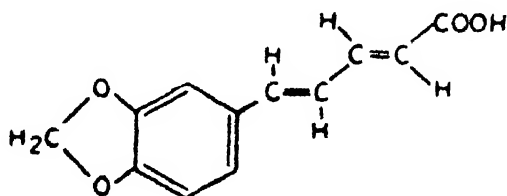
there is no free hydroxyl group in piperonylic acid (D) it is a methylene ether of proto-catechuic acid, i.e., it is 3, 4-methylenedioxybenzoic acid.



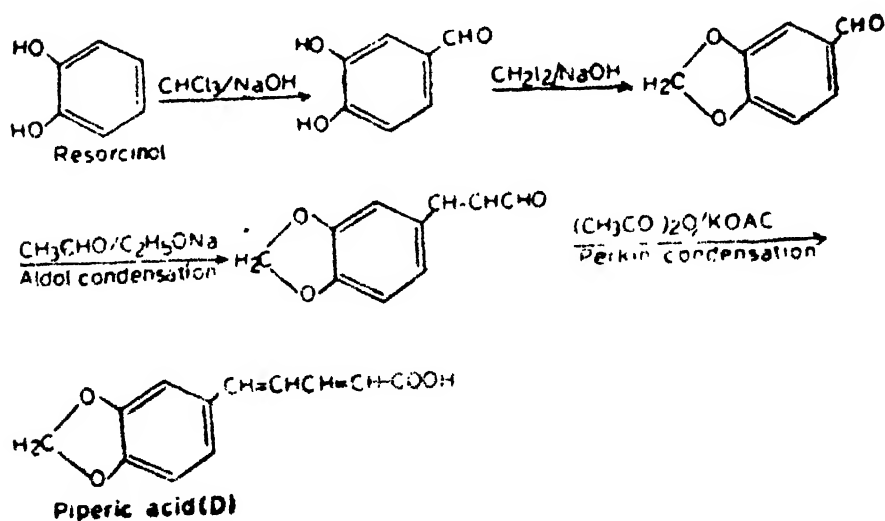
Piperonal (C), must be 3, 4—methylenedioxybenzaldehyde.



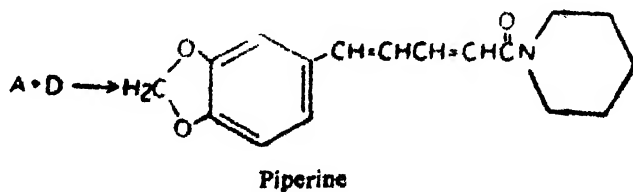
Formation of (C) and (D) suggests that piperine is a benzene derivative containing an unsaturated side-chain. Its structure may thus be conceived as the following:



5. This structure has been confirmed by its synthesis.



Piperidine (A) and piperic acid (D) can be condensed together via an amide linkage to give piperine.



25.8 COCAINE

Cocaine is the chief alkaloid in the leaves of the coca bush. It bears a structural relationship to atropine, an alkaloid found in belladonna and deadly night shade. Cocaine is also employed as a local anesthetic. Cocaine also has the ability of producing a feeling of well-being. It is, however, strongly narcotic and may lead to drug addiction by prolonged use.

Properties

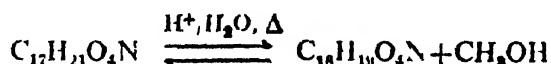
1 ()—Cocaine is a colorless, crystalline solid, m p. 98°, and is sparingly soluble in water.

2. It can be precipitated from solution of its salt by ammonia or sodium carbonate.

25.8.1 Constitution

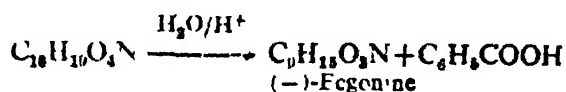
The elucidation of the structure of cocaine has been based on the following evidence:

1. Its molecular formula has been found to be $C_{17}H_{21}O_4N$.
2. Acid hydrolysis of cocaine furnishes methanol and a product called benzoyl ecgonine.



Benzoyl ecgonine has been shown to contain a $-\text{COOH}$ function. It thus appears that cocaine is the methyl ester of benzoyl ecgonine. This is further supported by the fact that esterification of benzoyl ecgonine with CH_3OH yields cocaine.

3. Benzoyl ecgonine can be further hydrolyzed by a mineral acid to ()—ecgonine and benzoic acid.

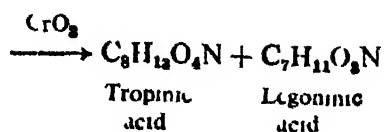


Establishment of the structure of ecgonine thus should provide a clue to the structure of cocaine.

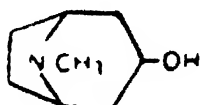
(i) Ecgonine, $C_9H_{15}O_3N$, contains a secondary alcoholic group, a carboxyl function and a tertiary nitrogen atom.

(ii) Oxidation of ecgonine forms the corresponding ketone ecgoninone which decarboxylates to tropinone. This latter substance oxidizes to tropinic and ecogonic acids.



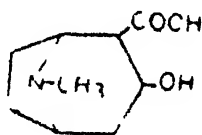


This oxidative degradation shows that ecgonine contains a tropane skeleton and that the secondary alcohol occupies the same position as in tropine



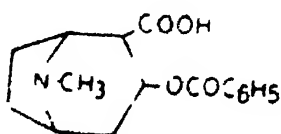
Tropine

Furthermore, facile decarboxylation of the ecgonine suggests that ecgonine is a β -keto acid, and has the following structure

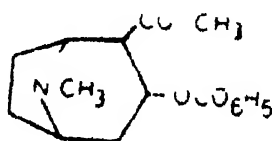


Ecgonine

From the above investigations the structure of benzoyl ecgonine and cocaine are the following

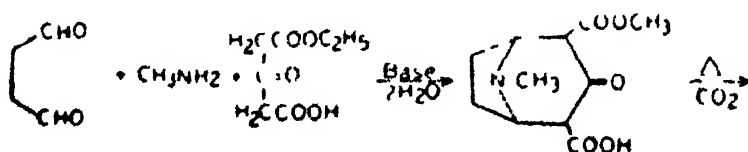


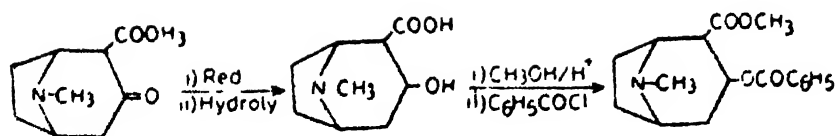
Benzoyl ecgonine



Cocaine

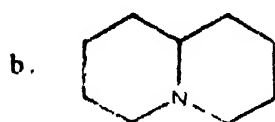
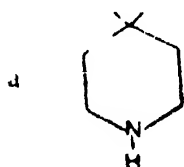
5. The structure of cocaine has been supported by its synthesis starting from succinaldehyde, methylamine and ethyl hydrogen acetonedicarboxylate.



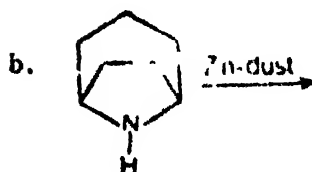
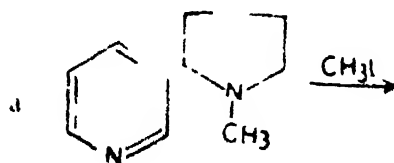


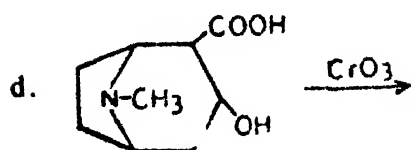
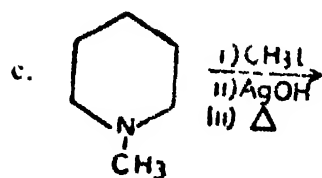
QUESTIONS

- 25.1 What are alkaloids? Describe the physiological properties of some of them.
- 25.2 What olefins would be obtained by Hofmann exhaustive methylation of the following amines.



- 25.3 Name some alkaloids containing quinoline and isoquinoline heterocycles.
- 25.4 Describe the general methods, with suitable examples, for the assignment of structures to alkaloids.
- 25.5 Discuss the evidences which resulted in the assignment of the structure of cocaine.
- 25.6 Predict the products of the following reactions.





25.7 Discuss the constitution of nicotine

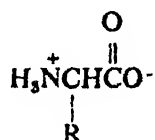
25.8 (a) Define an alkaloid. What are the general characteristics of alkaloids?

(b) Establish the structure of conine.

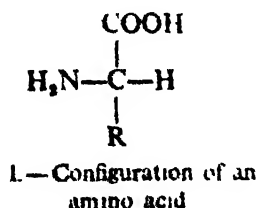
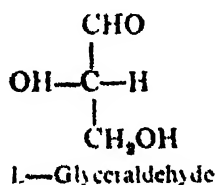
Amino Acids and Proteins

Apart from carbohydrates and fats, proteins constitute a major portion of human and animal nutrition. Amino acids represent one of the most important class of naturally occurring compounds. Many important parts of the body are made largely of proteins for example, muscle, blood cells and non-mineral parts of bones are proteins.

Enzymes and many hormones are proteins. Amino acids are obtained by the complete hydrolysis of proteins. As the name implies, *amino acids* are organic compounds and contain both an amino and an acid group and are amphoteric. They are all α -amino acids, i.e., the amino group is present on the α -carbon atom, the carbon next to the carboxyl carbon. The structure of an amino acid is usually written in a dipolar ion form, i.e., a 'zwitterion' or an internally ionized salt in which the amino group can accept a proton and the carboxyl group can donate one. Such a structure signifies the most amino acids are readily soluble in water but not soluble in organic solvents.



All amino acids have the same general formula as above but vary in the group R. About twenty five amino acids are found in appreciable quantities in proteins. Apart from glycine, in all naturally occurring α -amino acids the α -carbon is chiral and they are thus optically active. All those acids isolated from proteins, without exception, belong to the L-family and possess the following configuration at the α -carbon atom, i.e., corresponding to L-(-)-glyceraldehyde or *levo* glyceraldehyde.



This does not mean, however, that all such amino acids are *levorotary*, some are *levo* but others are *dextro*. Alanine, for instance, has the L-configuration but is *dextro* rotatory, therefore it is known as L(+)-alanine.

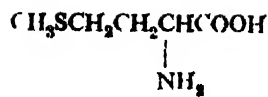
The direction of rotation of an amino acid varies with the change in pH of the solution. For instance L-serine is *levorotary* in distilled water but *dextro* rotatory in an acid solution.

In Table 26.1 α -amino acids isolated from protein hydrolysis are listed.

Table 26.1 Common Amino Acids

Name	Formula	Symbol	m.p. (°C)	Isoelectric point (pI)
<i>Neutral α-amino Acids</i>				
Glycine	$\text{H}_2\text{NCH}_2\text{COOH}$	Gly	233	5.97
L-(+)-Alanine	$\begin{array}{c} \text{H}_2\text{NCHCOOH} \\ \\ \text{CH}_3 \end{array}$	Ala	29	6.02
L-(+)-Valine*	$\begin{array}{c} \text{CH}_3\text{CH}(\text{CH}_3)\text{CHCOOH} \\ \quad \\ \text{CH}_3 \quad \text{NH}_2 \end{array}$	Val	15	5.9
I-(-)-Leucine*	$\begin{array}{c} \text{CH}_3\text{CH}(\text{CH}_3)\text{CH}_2\text{CHCOOH} \\ \quad \\ \text{CH}_3 \quad \text{NH}_2 \end{array}$	Leu	33	5.98
I-(+)-Iso-leucine*	$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CH}(\text{CH}_3)\text{CHCOOH} \\ \quad \\ \text{CH}_3 \quad \text{NH}_2 \end{array}$	Ileu	28	6.02
L-(-)-Serine*	$\begin{array}{c} \text{HOCH}_2\text{CH}(\text{NH}_2)\text{COOH} \\ \\ \text{NH}_2 \end{array}$	Ser	228	5.68
I-(-)-Threonine*	$\begin{array}{c} \text{CH}_3\text{CH}(\text{OH})\text{CH}(\text{NH}_2)\text{COOH} \\ \quad \\ \text{OH} \quad \text{NH}_2 \end{array}$	Thr	253	5.60
I-(-)-Phenyl-alanine*	$\begin{array}{c} \text{C}_6\text{H}_5\text{CH}_2\text{CH}(\text{NH}_2)\text{COOH} \\ \\ \text{NH}_2 \end{array}$	Pha	283 (dec)	5.84
L-(-)-Cystine	$\begin{array}{c} \text{S}-\text{CH}_2\text{CHCOOH} \\ \quad \\ \text{NH}_2 \quad \text{NH}_2 \\ \text{S}-\text{CH}_2\text{CHCOOH} \\ \\ \text{NH}_2 \end{array}$	Cys (S)	260	5.06

L-(+)-Methionine

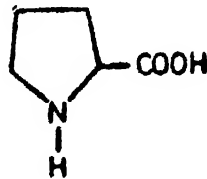


Met

283

5.06

L-(-)-Proline

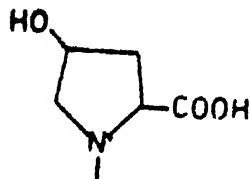


Pro

299

6.30

L-(-)-Hydroxyproline

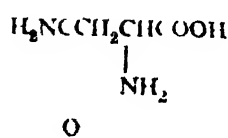


Hyp

270

6.33

L-(+)-Asparagine

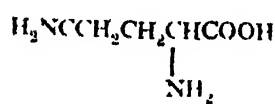


Asp(NH₂)

237

5.41

L-(+)-Glutamine

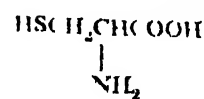


Glu(NH₂)

185

5.70

L-(-)-Cysteine

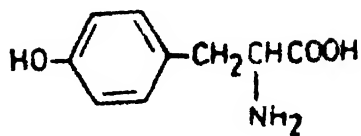


C

178

5.02

L-(-)-Tyrosine



Tyr

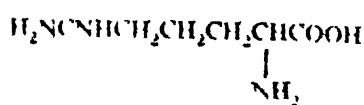
344

5.37

Basic α-Amino Acids

NH

L-(+)-Arginine*

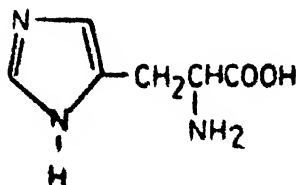


Arg

238

10.76

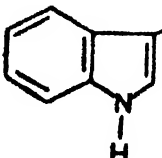
L-(-)-Histidine*



His

277

7.59

L-(+)-Lysine*	$\text{NH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{COOH}$	Lys	224 (dec)	9 74
L-(-)-Tryptophan*		Try	382	5 88

Acidic α -Amino Acids

L-(+)-Aspartic acid	$\text{HOOCCH}_2\text{CH}(\text{NH}_2)\text{COOH}$	Asp	270	2 98
L-(+)-Glutamic acid	$\text{HOOCCH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{COOH}$	Glu	219	3 31

***Essential Amino Acids**

with the symbols used for their designation. They belong to the aliphatic, aromatic and heterocyclic series depending upon the nature of R. Amino acids are classified into three types according to their electrochemical characters.

Neutral Amino Acids Most α -amino acids contain one amino and one carboxyl group and are termed as neutral amino acids (Monoaminomonocarboxylic acids), for example, alanine, leucine, valine, tryptophan, etc.

Basic Amino Acids These are others that contain an extra amino group and are known as basic amino acids—(Diaminomonocarboxylic acids), for example, lysine, arginine and histidine.

Acidic Amino Acids Those containing an extra carboxyl group are referred to as acidic amino acid (Monoaminodicarboxylic acids) for example, aspartic and glutamic acids.

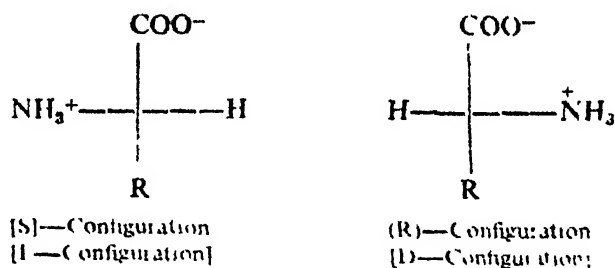
Amino acids are essential for the growth of the body, for tissue building and for the protection of body from disease.

Amino acids are of great biological importance, certain α -amino acids must be present in the diet of humans for normal growth as they are not synthesized by the body. Such α -amino acids that are indispensable to life are referred to as *essential amino acids*. The omission of any of the essential amino acids from the diet leads to one or more manifestations of malnutrition. In the Table, above, these acids are indicated by an *asterisk*. Other amino acids can be adequately synthesized in the body. Amino acids

may be classified as α , β or γ according to the position of the amino group in the carbon chain. Besides these there are other naturally occurring amino acids such as β -alanine, γ -aminobutyric acid etc., but are not found in proteins.

26.1 PHYSICAL PROPERTIES OF AMINO ACIDS

Amino acids are white, crystalline solids. Most of them are quite soluble in water. Since they exist in dipolar forms, amino acids have high melting points (usually above 200°), even though their molecular weights are low. That amino acids exist as dipolar ions in neutral aqueous solution is also indicated by their high dielectric constants and large dipole moments, which are reflections of the occurrence of both positive and negative charge in the same molecule. They contain one asymmetric center, threonine and isoleucine have two; and thus are optically active and exist in *d*- and *l*-enantiomeric forms. All naturally occurring amino acids found in proteins belong to the L-series. The α -amino acids in proteins are usually of the (S)-configuration. (R)-configuration amino acids do not occur in most living systems.



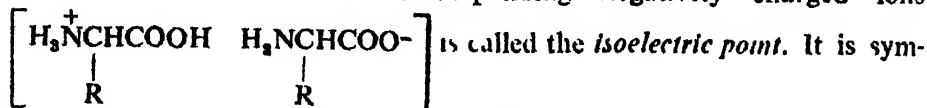
The determination of the relative configuration of amino acids has been one of the principal accomplishments of synthetic organic chemistry. For this purpose, the groups linked to the chiral carbon had to be modified in a known manner without changing the configuration about this carbon. This necessitated the use of ingenious chemical reactions in which the mechanism of the reaction was also precisely known.

Amino acids are amphoteric and they exist as dipolar ion in dry solid state. In aqueous solution, however, there is an equilibrium between the dipolar ion and the anionic and cationic forms of the acids



Depending on the pH of the solution the amino acids can exist in either form. At low pH the amino acids are present as cations and at high pH as anions. The pH at which positively charged amino acids are present in

equal concentration to the corresponding negatively charged ions



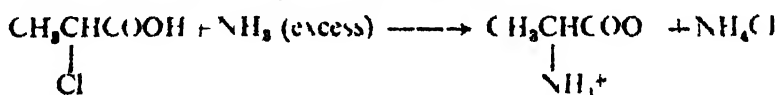
bolized by PI. At the pI point the negative charge exactly balances the positive charge and the acid does not migrate to either electrode when placed in an electric field. The PI value varies for different α -amino acids and it provides a method for the separation of the acids. α -Amino acids are generally less soluble at the pI point.

26.2 SYNTHESIS OF α -AMINO ACIDS

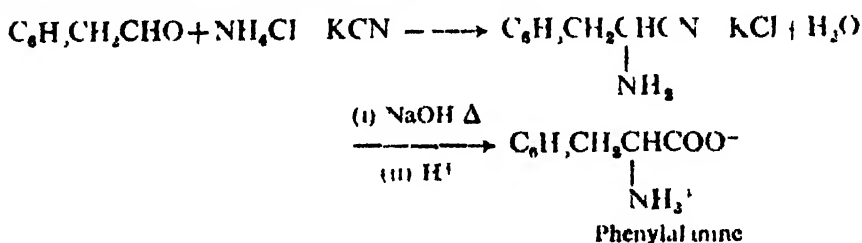
Generally most simple amino acids have pI values in the range 5 to 6.5. Acidic amino acids have pI of about 3 while pI of basic amino acids is 10 or higher.

Amino acids are nowadays commercially available in the market. They may be prepared by the following representative methods:

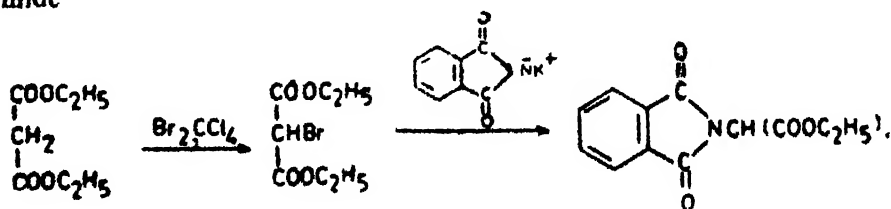
1 *Amination of α -Halo Acids.* Reaction of an α -halo acid, obtained by the Hell-Volhard-Zelinsky reaction, with ammonia or an amine is a convenient method for preparing an amino acid. In this method the separation of α -amino acid from NH_4Cl is often difficult.



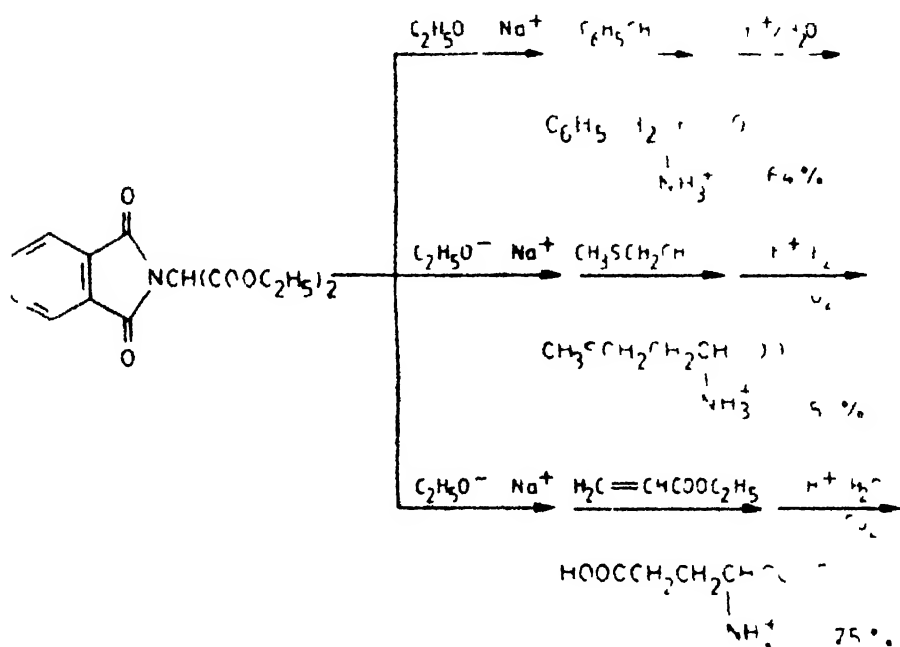
2 *The Strecker Synthesis.* It has been one of the predominant methods for the preparation of amino acids. According to this, an aldehyde is treated with ammonium chloride and potassium cyanide to yield an amino nitrile which on subsequent hydrolysis forms the acid.



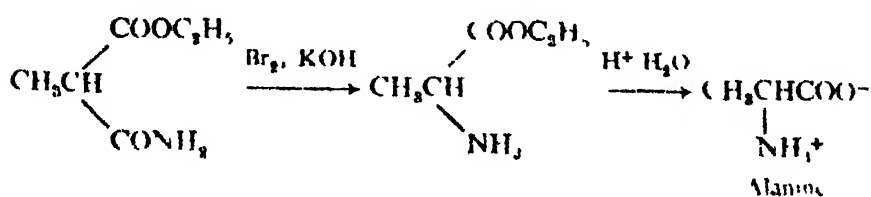
3 *Alkylation of N-substituted Aminomalonic Ester.* It is a general method for the preparation of α -amino acids. N-phthalimidomalonic ester is first obtained by reacting bromomalonic ester with the potassium salt of phthalimide.



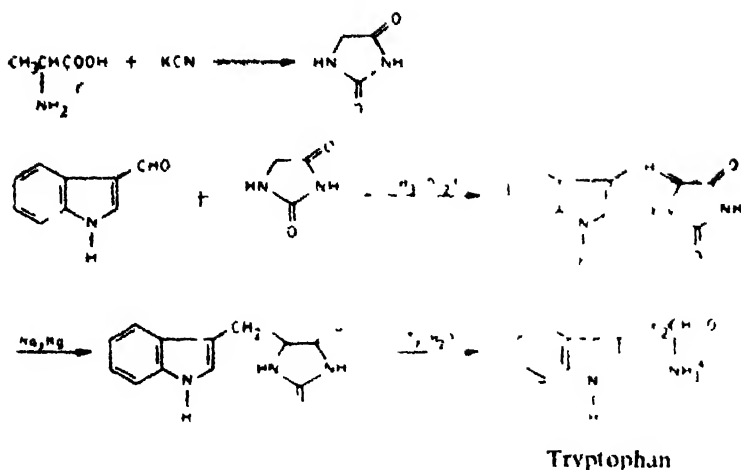
This product can then be alkylated by a variety of alkyl, halides or α , β -unsaturated carbonyl compounds. The resulting compounds, on hydrolysis and subsequent decarboxylation leads to α -amino acids. It is illustrated by the following examples:



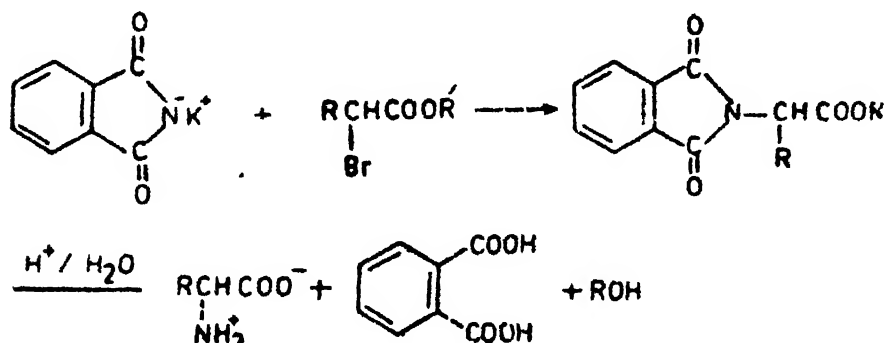
4 *Hofmann Degradation* Substituted malonic ester amides undergo Hofmann degradation and the resultant product on hydrolysis yields an α -amino acid



5. *Hydantoin Synthesis* Hydantoin itself is prepared by treatment of glycine with KCN ; the active methylene group can then be condensed with aldehydes and the desired product obtained by reduction and hydrolysis. This synthesis is illustrated for the preparation of tryptophan



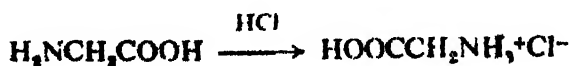
6. *The Gabriel Phthalimide Synthesis:* The potassium salt of phthalimide on reaction with an α -halo ester followed by hydrolysis of the resultant product leads to an α -amino acid. If R is hydrogen then the product is glycine. Phthalimide is recoverable in the form of phthalic acid, which is converted to phthalimide by reaction with ammonia and used again



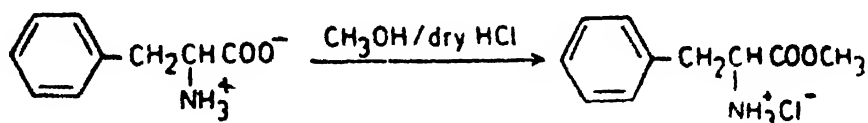
26.3 REACTIONS OF α -AMINO ACIDS

Like any other organic compound containing more than one type of functional group, the α -amino acids undergo reactions characteristic of both the amino and carboxyl groups

1. *Salt Formation:* Amino acids form salts both with mineral acids, due to the protonation of the amino group, and with strong bases.

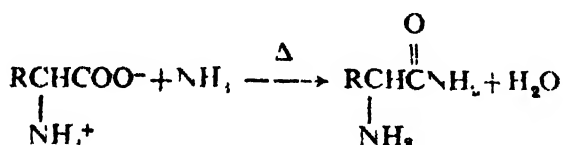


2. *Esterification*: α -Amino acids can react with alcohols to form α -amino esters. The amino acid is suspended in alcohol and dry hydrogen chloride is

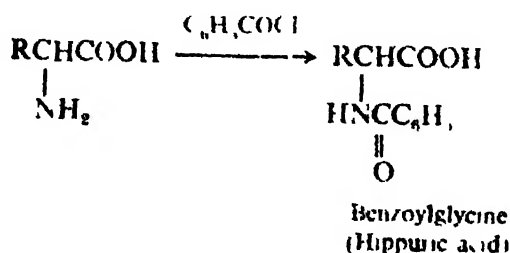
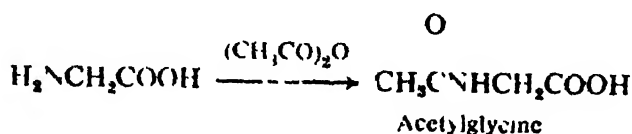


passed through the solution. The amino ester precipitates as its hydrochloride.

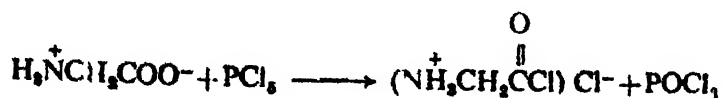
3. *Amide Formation*: An amino acid reacts with ammonia to yield an amide.



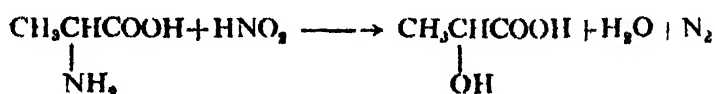
4. *Reaction with Reactive Acid Derivatives*: The amino group of α -amino acids reacts with acid anhydrides or acid chlorides to form acyl derivatives.



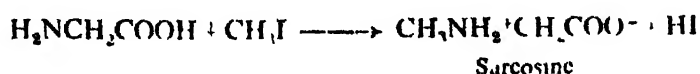
5. *Reaction with PCl_5* : On treatment of an α -amino acid with phosphorus pentachloride, a hydrochloride of the chloride of the amino acid is obtained.



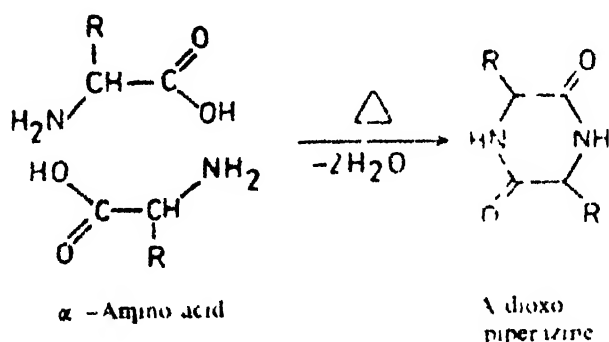
6. *Action of Nitrous Acid:* With nitrous acid, an α -hydroxy acid is obtained with the evolution of nitrogen.



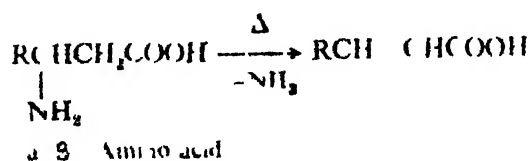
7. *Alkylation of the Amino Group.* An amino acid may be alkylated at the amino group with an alkyl halide



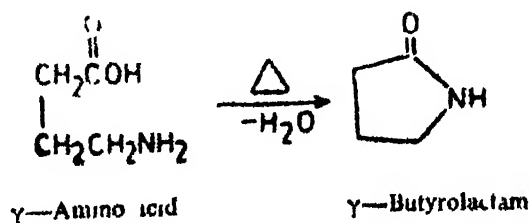
8. *Action of Heat* This is an important reaction different amino acids form different compounds. A cyclic diamide is obtained from an α -amino



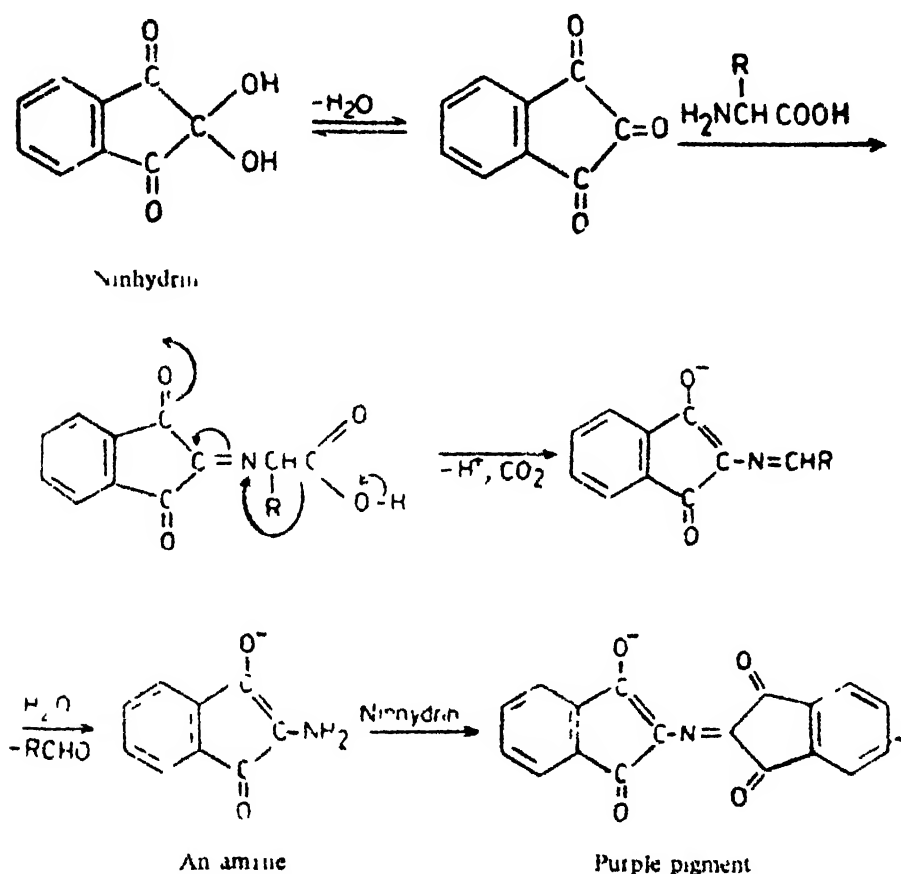
acid. β -Amino acids lose ammonia to form α, β unsaturated acids



A γ -amino acid is easily converted to a lactam by loss of water

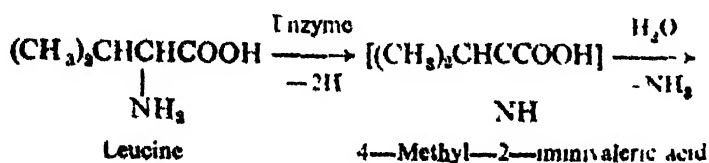


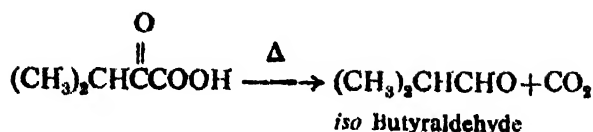
9. *Reaction with Ninhydrin*: The quantitative analysis of α -amino acids is based on their reaction with ninhydrin (triketohydrindene hydrate). This reaction involves both the amino and carboxyl groups of the amino acid. On heating, an α -amino acid with two molecules of ninhydrin forms an intensely colored product



A purple color is given by all amino acids having a free amino group. In contrast, proline and hydroxyproline give a yellow pigment because the α -amino group is substituted in these acids.

10. *Oxidation Deamination*: An amino acid, by the catalytic action of enzymes, is oxidized to an intermediate α -imino acid which is readily hydrolyzed to the corresponding α -keto acid



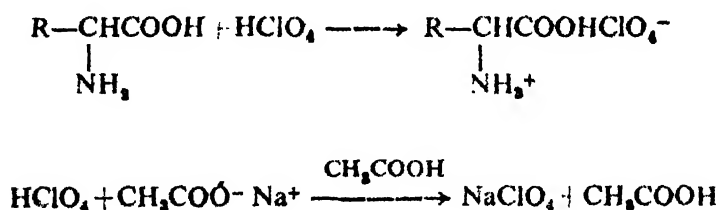


The ammonia reacts further to give the purple pigment and the α -keto acid decarboxylates to an aldehyde.

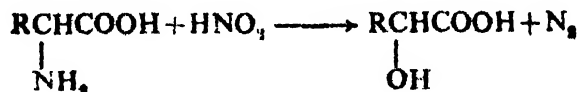
26.4 DETERMINATION OF AMINO ACIDS

Hydrolysis of proteins with acid gives a mixture of amino acids. The mixture can be separated into individual components by a number of techniques namely paper chromatography, ion-exchange resins, selective precipitation, etc. The first of these, i.e., paper chromatography is a very useful technique for identifying the components. Several other techniques are also available for the determination of amino acids.

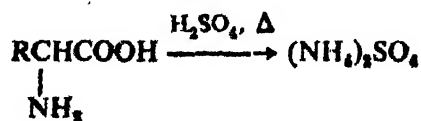
An amino acid can be directly titrated as a base in acetic acid. The amino acid is treated with a known volume of perchloric acid (HClO_4) and the excess acid is back-titrated with sod. acetate using phenolphthalein as indicator. The following reactions take place :

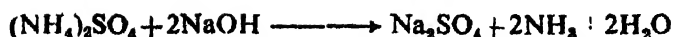


The nitrogen content present in the form of a primary amino group ($-\text{NH}_2$) can be determined by the *Van Slyke method*. The acid is treated with nitrous acid and the volume of nitrogen liberated is measured.



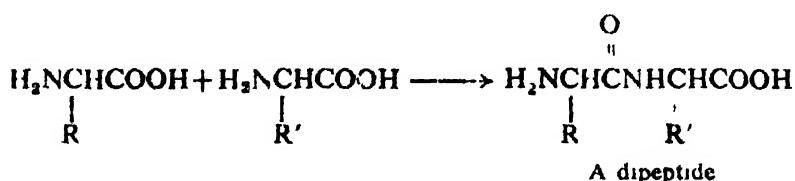
The total nitrogen content may also be determined by *Kjeldahl determination*. In this method the organic compound is digested with conc. sulfuric acid and a catalyst. The ammonium salt thus formed is converted into ammonia with NaOH which is distilled over and titrated against a standard acid.



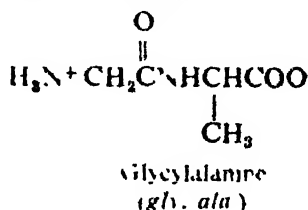


26.5 POLYPEPTIDES

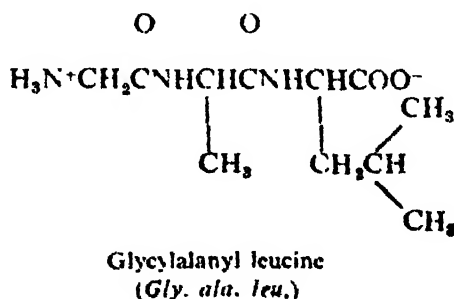
An α -amino acid contains both an amino and a carboxyl group and an intermolecular reaction can take place between these two groups to give an *amide* or a *peptide* linkage.



Peptides are polyamides that contain between 2 to 100 units of amino acids. A peptide contains a free —COO^- group (called C-terminal end) and a free —NH_3^+ group (called N-terminal end) at the terminal positions. Peptides are named according to the number of amino acid residues, thus a dipeptide has two amino acids, a tripeptide has three and so on. Substances that contain more than ten amino acid residues are called *polypeptides*. It is generally accepted that molecules containing more than 100 amino acid residues (mol weight $\sim 10,000$) are classified as *proteins*. *Peptides* are named beginning with the N-terminal end and writing the constituent amino acids. The following dipeptide is named as follows.



Another example is:

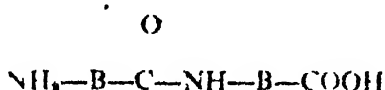
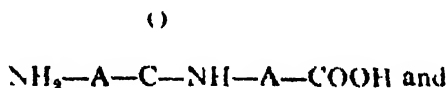


Peptides and proteins can be synthesized in the laboratory. The principal aim is to form an amide linkage by condensing an amino group of one acid with the carboxyl function of the other. The formation of a peptide linkage

between two amino acids is an endothermic reaction, i.e., it requires the application of energy. As a result, high energy starting materials such as acid chlorides or azides are employed so that they can react with the amino acids by an exothermic reaction. Normally an amide linkage is formed by converting an acid into its chloride and subsequent treatment with ammonia. Amino acids, however, cannot be converted into the acid chloride in this manner as polymerization takes place. Moreover, amino acids like lysine, threonine, etc., which contain additional functional groups cause difficulties through side-reactions. But such problems have been taken care of and general methods for the synthesis of peptides have been devised.

The synthesis of peptides involves the formation of amide linkages, but the difunctional nature of amino acids has necessitated the development of highly selective reagents. The use of such reagents is essential to prevent the reaction between two molecules of the same acid. One acid molecule functions as the acylating agent and attacks the amino group of the second

molecule. For example, if the peptide $\text{NH}_2\text{—A—}\overset{\text{O}}{\parallel}\text{C—NH—B—COOH}$ has to be prepared from $\text{NH}_2\text{—A—COOH}$ and $\text{NH}_2\text{—B—COOH}$, then it is necessary to block the amino group of A and the carboxyl group of B before condensation, else products like the following



may also be formed. The protecting group should be such that it can be removed easily after peptide formation.

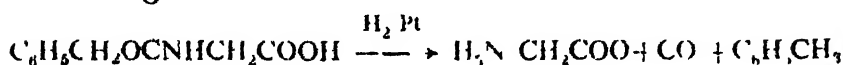
(i) *Protection of the Amino Group*: The synthesis of a polypeptide involves a successive condensation of the amino group of one amino acid with the carboxyl group of a second amino acid. As stated earlier there is a strong possibility of self-condensation of similar amino acids. To avoid this the amino group is protected by its reaction with a suitable reagent so that the condensation of the carboxyl group of this acid can occur only with a different amino acid. The protecting group is then removed after peptide formation. An amino group can be protected by reagents such as carbobenzoxy chloride (removed by catalytic hydrogenation, H_2/Pd), phthalic anhydride (removed by treatment with hydrazine at 25°), *p*-toluenesulphonyl chloride (removed by means of Na in liquid ammonia), triphenylmethyl chloride (removed by mild acid hydrolysis), trifluoroacetic anhydride (removed by

mild base hydrolysis), and *t*-butylazido formate (removed in the presence of an acid), etc. The reagents employed for the removal of the protecting groups do not affect the peptide bond

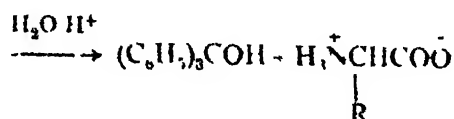
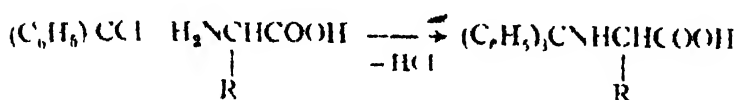
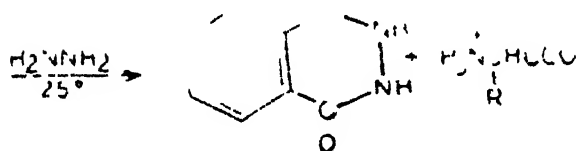
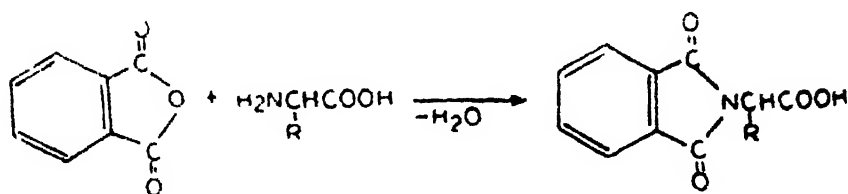
(i)



(ii)

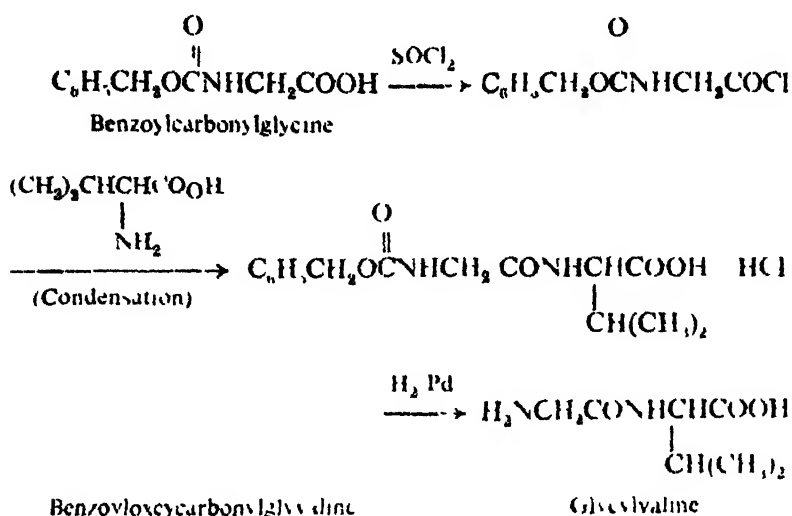


Benzylloxycarbonyl glycine

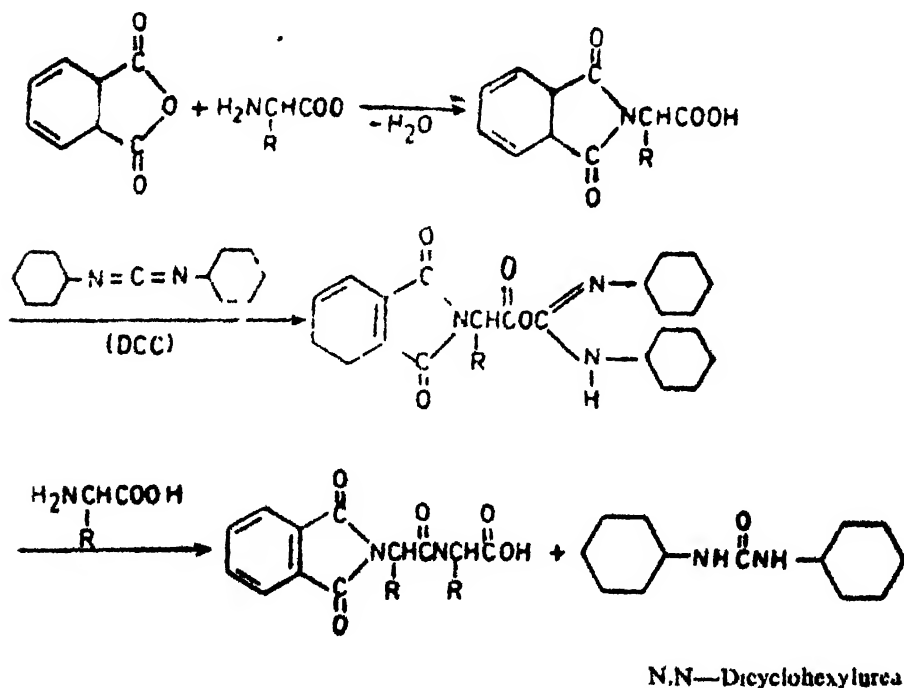


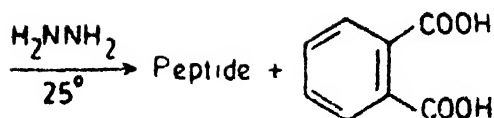
(ii) *Activation of the Carboxyl Group* A carboxyl group can be protected by forming its ester, i.e. methyl, ethyl, benzyl or *p*-nitrophenyl. However, activation of the free carboxyl (or amino) group is essential for the formation of a peptide linkage. This step should be carried out prior to condensation with another amino acid. This can be done by converting a carboxyl group into acyl azide ($-\text{CO}-\text{N}_3$), acyl chloride ($-\text{CO}-\text{Cl}$), or the anhydride ($-\text{CO}-\text{O}-\text{COR}$). The formation of the amide bond starting from a carboxyl group and an amine is an endothermic process, consequently this reaction cannot be expected to give good yields of the product. To increase

yields, the process of activation where the carboxyl group is converted into a high energy molecule is carried out by forming an acid azide, chloride, etc. Due to its energy, the reaction of the activated carboxyl group with the amine to give the peptide bond now gives an exothermic reaction, thus better yields can be obtained.

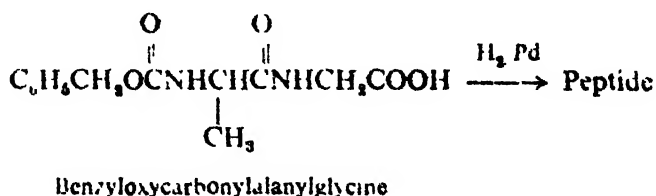
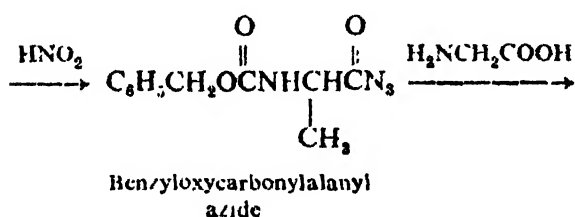
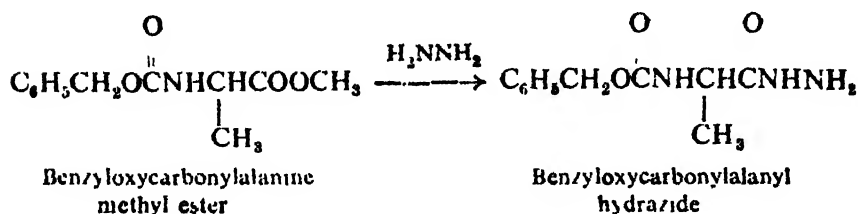


The activation process can be a part of a single operation as in the case of dicyclohexylcarbodiimide (DCC).

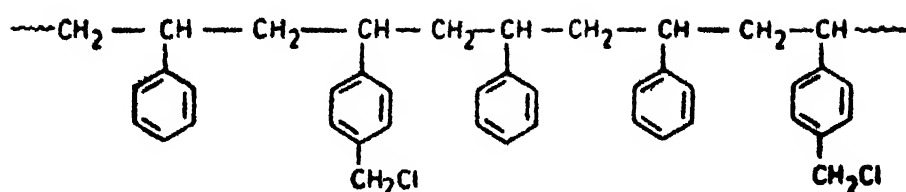
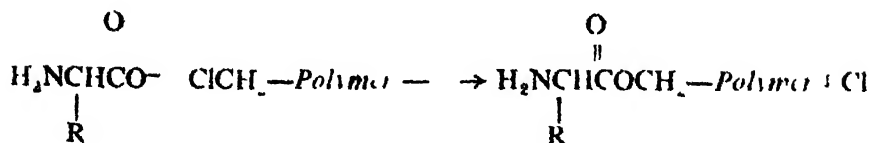




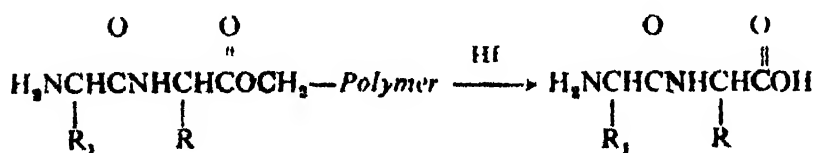
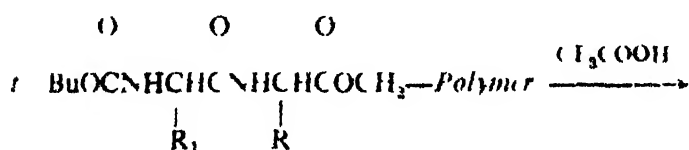
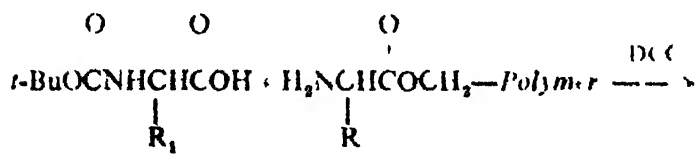
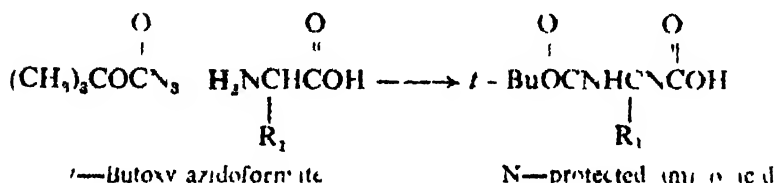
Another method for coupling of two amino acids involves activation of the carboxyl group by conversion into an acylazide. A typical nucleophilic reaction occurs when acyl azide is treated with an amino acid in alkaline solution.



Solid Phase Method (Merrifield Method): A recent technique for the synthesis of polypeptides was devised by R B. Merrifield and coworkers. The peptide, according to this method is synthesized on the surface of an insoluble polymer. One of the common polymers used is polystyrene in which some of the benzene rings are chloromethylated, i.e., linked to $-\text{CH}_2\text{Cl}$ group. The polymer is cross-linked with about 2% of divinylbenzene. This polymer may be designated as $\text{ClCH}_2\text{—Polymer}$. The C—terminal end of the amino acid is bound to the polymer by shaking a basic solution of the amino acid in ethyl acetate with the insoluble polymer. An $\text{S}_{\text{N}}2$ attack of the carboxylate ion takes place at the benzyl carbon removing the halogen and the result is a polymer—bound amino acid derivative. This polymer derivative is

Insoluble Polymer, $\text{ClCH}_2\text{—Polymer}$ 

Polymer—bound amino acid derivative

 $\text{HCH}_2\text{—Polymer}$

then condensed with an N—protected amino acid using dicyclohexylcarbodiimide (DCC). The amino acid gets attached to the growing peptide and the latter is separated by filtration. The protecting group is removed by adding a strong anhydrous acid, usually trifluoroacetic acid. This process is repeated by adding another N—protected amino acid followed by condensation in the

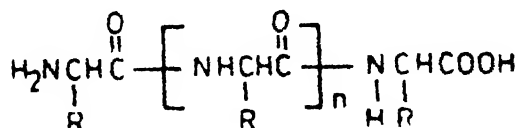
presence of DCC. After the desired polypeptide is built it is removed from the resin by adding anhydrous hydrogen fluoride. This does not affect the peptide bond. The synthetic peptide is eventually purified by a suitable chromatographic method.

The Merrifield method is very efficient and polypeptides containing a large number of amino acids can be prepared in good yields. Furthermore, since the process involves the repetition of a small number of simple and similar steps, this can be carried out by an automatically programmed machine.

Merrifield and coworkers synthesized the nonapeptide bradykinin by this automated procedure with an overall yield of 85%. They also synthesized bovine pancreatic ribonuclease containing 124 amino acids, the first protein to be synthesized artificially from its amino acid components.

26.6 PROTEINS

Proteins (from *protios*, Greek for, of the first rank) are complex organic molecules containing nitrogen as well as carbon, hydrogen, oxygen and frequently other elements like sulfur too. Proteins occur in every part of plant and animal organisms and are the major constituent of skin, hair, muscle, blood, nails, horns, etc. In plants they are found principally in the seeds. Blood is about 80% water; the remaining 20% is largely protein. Almost all biochemical reactions need enzymes as catalysts for them to proceed at a rate sufficient to maintain life. The enzymes are basically proteins though they may contain other compounds. Certain proteins such as hormones and gene regulators direct and control all forms of body repair, construction and energy conversions. No other class of compounds is associated in such a variety of functions that are essential to life as proteins. Proteins are polyamides and α -amino acids are the monomer units; they usually have a free carboxylic group at one end and a free amino group at the other end.



The isolation and purification of proteins is far more difficult than for most organic compounds. Proteins are very unstable and very difficult to obtain unchanged from their source. There are infinite number of proteins possible due to the numerous ways in which the amino acids can be linked to each other. The molecular weights of proteins are very high but on acid hydrolysis they all yield a group of simple organic compounds of low molecular weight, the α -amino acids. In protein molecules, the amino acid residues are covalently linked to form long chains. They are bonded in head-to-tail arrangement through substituted amide linkages called peptide bonds. Proteins are divided into two major classes on the basis of their compositions.

simple and conjugated. Simple proteins are those which on hydrolysis yield only amino acids and no other major organic or inorganic products such as albumins, glutenins, globulins, etc. Conjugated proteins yield not only amino acids but also other organic or inorganic products examples are, glycoproteins, lipoproteins, phosphoproteins, etc.

26.6.1 General Physical Properties

Most of the proteins are colorless, tasteless, and insoluble in water, alcohol and ether. They possess high molecular weights and are optically active (*levorotatory*). The proteins structure can be disrupted on heating, on treatment with mineral acids or on exposure to light. This process is called *denaturation*. It is the sensitivity of proteins to denaturation that makes its isolation difficult.

26.6.2 Chemical Properties

1. Proteins form salts with bases. Casein, for instance, is present in milk as its calcium salt.

2. On acid or enzymatic hydrolysis, of proteins amino acids are formed. Digestive enzymes hydrolyze proteins to peptides and amino acids which are absorbed and transferred by the blood to various body tissues.

3. Proteins respond to several color tests:

a. With ninhydrin, a purple color is produced.

b. Millon's reaction yields a pink color.

c. A yellow color is obtained with iodine.

Examples of some selected proteins along with their sources of extraction are given in Table 26.2.

Table 26.2 Selected Proteins and their Sources

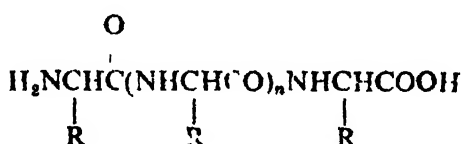
Protein	Mol. weight	Source
1. Insulin	5,700	Pancreas
2. Ribonuclease	12,600	Pancreas
3. Myoglobin	16,900	Horse heart
4. Chymotrypsinogen	23,200	Bovine
5. β -lactoglobulin	35,400	Milk
6. Zein	40,000	Corn
7. Fibroin	56,000	Silk
8. Hemoglobin	64,500	Human
9. Hexokinase	102,000	Yeast
10. Glutenin	120,000	Wheat

26.6.3 Structure of Proteins

The determination of structure of a polypeptide or protein involves a number of steps.

(i) *The Amino Acid Analysis*: If the polypeptide chains are covalently cross-linked by one or more disulfide bonds, these must be cleaved by appropriate chemical reactions. A common method is oxidation using performic acid. Once the polypeptide chain has been obtained in a homogeneous form, it is completely hydrolyzed to determine the amino acid composition. Peptide bonds, for this purpose are hydrolyzed by heating with 9N HCl, are then subjected to chromatographic analysis. The analytical method commonly employed to composition is automated ion—exchange chromatography in an amino acid analyzer.

(ii) *Identification of the N-Terminal Residue*: Peptides may be considered to be substituted amides; in which one end terminates in free —NH_2 group and the other in free —COOH group. These are referred to as N—terminal and C—terminal residues respectively.



The N—terminal residue is determined by two methods, one is known as the *Sanger method* and the second as the *Lüman degradation*. According to the first method, the free α —amino group reacts with 2,4—dinitrofluorobenzene (DNFB) to form a yellow derivative. This derivative is hydrolyzed and a mixture of amino acids is obtained of which only one is labeled with 2,4—dinitrofluoro group. From this labeled amino acid one can determine which amino acid is located at the terminal position. In the Edman method, the free α —amino group of the peptide is allowed to react with phenylisothiocyanate to afford the corresponding phenylthiocarbamoyl peptide. This derivative is then treated with anhydrous HCl; the N—terminal residue is split off as a phenylthiocarbamoyl amino acid which cyclizes to the corresponding phenylthiohydantion derivative. This is then identified by gas—liquid chromatograph (glc).

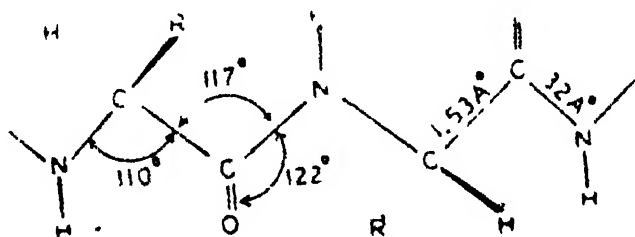
(iii) *Identification of the C—Terminal Residue*: The C—terminal amino acid of a peptide can be selectively removed by the action of the enzyme *carboxypeptidase*, which specifically attacks the C—terminal peptide bond.

(iv) *Peptide Fragmentation*: A number of methods may be used to fragment a polypeptide or protein into smaller units. The most useful method,

however, is enzymatic hydrolysis and several of such enzymes are available for this purpose such as *pepsin*, *trypsin*, etc. Nowadays, there are four types of structures that can be associated with proteins.

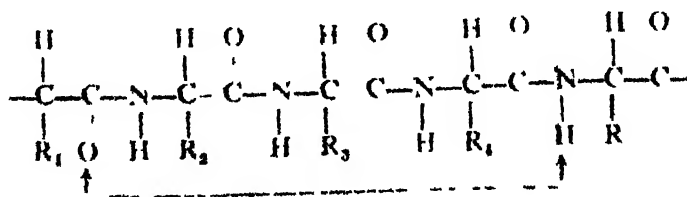
Primary Structure: This refers to the covalent backbone of the polypeptide chain and the sequence in which the amino acids are connected along the chain. The determination of primary structure employs the same experimental procedure as are used for the peptides. The elucidation of the amino acid sequence of a protein was first successfully established for insulin by F. Sanger. The establishment of the primary structure of other proteins such as myoglobin, trypsin, hemoglobin, etc. quickly followed.

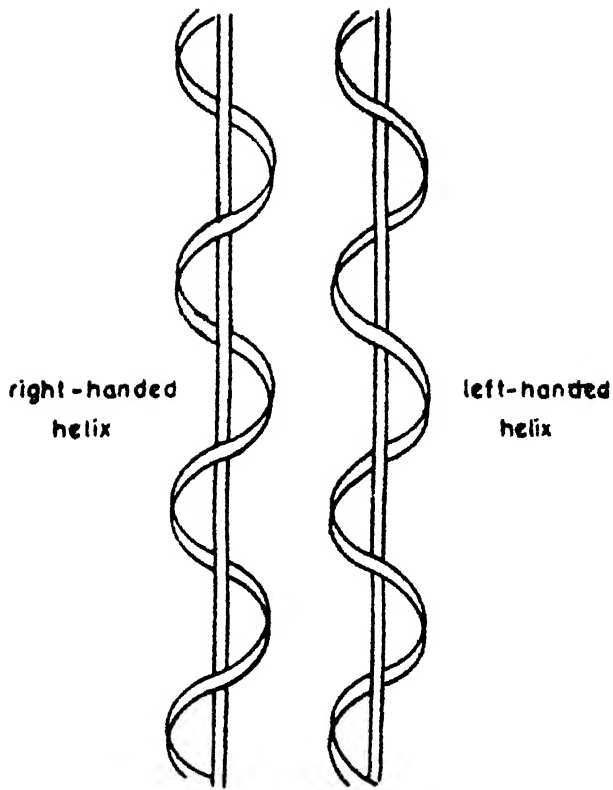
Secondary Structure: This type of structure refers to a regular recurring or a systematic arrangement in space of polypeptide chain. Linus Pauling and R. B. Corey, by a careful X-ray crystallographic study showed that the peptide bond was a rigid planar structure. The hydrogen atom of —NH— group is nearly always *trans* to the oxygen of the carbonyl group as shown below.



Moreover, there is no freedom of rotation about the C—N bond of the peptide, as this bond has a partial double bond character. Pauling proposed that a protein can fold itself in two ways (i) α -helix and (ii) a pleated sheet.

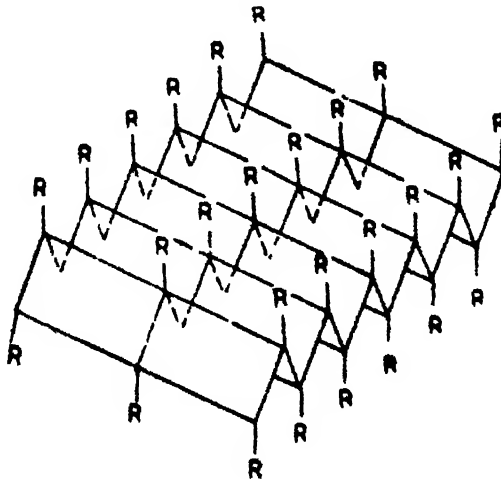
The α -helix is a spiral that can be either right-handed or left-handed. The tightly coiled polypeptide main chain forms the inner part of the rod and the side-chains extend outward in a spiral form. The α -helix is stabilized by H-bonding between NH and CO groups of the main chain. The CO group of each amino acid is hydrogen-bonded to the NH group of the amino acid that is situated for residues ahead in the linear sequence.





The stability of the coil is governed by the nature of the side-chain groups and their sequence along the chain, for example, proline residues destabilize the α -helical structure.

The β -pleated sheet differs markedly from the α -helix in that it is a sheet rather than a rod; the polypeptide chain is fully extended rather than being tightly coiled as in α -helix



The second important difference is that the β -pleated sheet is stabilized by H-bonding between CO and NH groups in different polypeptides, whereas in the α -helix the H-bonds occur between CO and NH groups in the same polypeptide chain. The secondary α -helix structure is particularly common in *keratins* which are *fibrous* proteins of hair and wool. Extension of the β -pleated sheet structure has been found in *silk fibrogin* secreted by the silk-worm *Bombyx mori*.

Tertiary Structure: This refers to how the polypeptide chain is bent or folded in three dimensions as to form the compact and tightly folded structure. This structure is far more complex than primary and secondary structures because the polypeptide chains of proteins are not arranged along one axis but are irregularly and compactly folded.

Quaternary Structure: This type of structure refers to how individual polypeptide chains of a protein having two more chains are arranged in relation to each other. For example, hemoglobin is composed of four polypeptide chains linked together non-covalently.

26.6.4 Role of Proteins and Enzymes in Biological Processes

The biological processes are extremely diverse and various proteins have a different role to play. Proteins are vital for the living organisms. They constitute an essential component of animal and human diet. A few functions of some specific proteins may be described here. *Hemoglobin* acts as an oxygen carrier from lungs to the tissues, *nucleoproteins* form the important constituents of the cells that supply and transmit genetic message in cells, *sperm albumin* binds free fatty acids tightly, *lipoprotein* of blood plasma transport lipids between the intestine, liver and adipose (fatty) tissues. The blood proteins *thrombin* and *fibrinogen* participate in blood clotting and thus prevent the loss of blood. Many of the hormones such as *insulin* and *thyroxine* which are proteins regulate various metabolic processes in the body.

An enzyme is a naturally occurring catalyst. A *catalyst* is a substance which provides energy and thus makes the reactions go faster. Louis Pasteur recognized that fermentation is catalyzed by enzymes. Today approximately 2,000 different enzymes are known, many of them have been isolated in pure state. Many enzymes are named by putting a suffix *ase* to the name of the substrate which they catalyze. For instance, *urease*, catalyzes urea to ammonia and carbon dioxide, *phosphatase* catalyze the hydrolysis of phosphate esters. Some enzymes are given chemical names such as trypsin or pepsin. Many enzymes, in addition, to a protein part contain a non-protein component called the *prosthetic group* or *coenzyme*. Enzymes work under mild conditions and are extremely specific about the reaction that they catalyze.

In other words, a given enzyme attacks a particular substrate only. The enzyme catalyzed reactions are much more faster than the corresponding uncatalyzed ones.

QUESTIONS

- 26.1 Define the following:
A prosthetic group, conjugated protein, a dipeptide and enzymes.
- 26.2 Write structures of (a) any two naturally occurring neutral α -amino acids (b) any two naturally occurring basic α -amino acids (c) any two naturally occurring acidic α -amino acids.
- 26.3 In an alkaline solution, glycine, $\text{H}_2\text{NCH}_2\text{COO}^-$, has two basic groups. What products would form on the addition of 1 equivalent of acid? 2 equiv? and 3 equiv?
- 26.4 A naturally occurring amino acid forms a monoacetyl derivative with excess acetic anhydride, but treatment with nitrous acid yields no nitrogen. Suggest a structure for this compound.
- 26.5 How will you distinguish between the following pairs chemically?
 - a. Serine and threonine
 - b. Glycine ethyl ester and valine
 - c. Phenylalanine and acetylphenylalanine
 - d. Aspartic acid and malic acid
- 26.6 Why does proline give a yellow color toward ninhydrin?
- 26.7 Why is it necessary to protect the amino group of α -amino acids in polypeptide synthesis?
- 26.8 Describe the solid phase method for the synthesis of polypeptides. Why is it so useful?
- 26.9 What are amino acids and how are they related to proteins? Give three methods employed for the preparation of amino acids? Describe giving equations, the action of heat on α , β —and γ —amino acids.
- 26.10 State giving equations, the chemical properties of amino acids in which:
 - a. Only an amino group is involved
 - b. Only a carboxyl group is involved
 - c. Both the groups are involved
- 26.11 a. What are proteins. How are amino acids related to them? Describe the important properties and reactions of proteins.
b. Describe the methods of preparing pure amino acids. Since the behaviour of α , β —and γ —amino acids on heating.

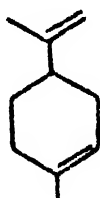
- 26.12 What are peptides, proteins and enzymes? What is their importance in biological processes?
- 26.13 a. What are amino acids and how are they related to proteins? Give three methods for the preparation of amino acids.
b. Describe one method for the preparation of artificial silk.
- 26.14 a. What are essential amino acids? Name two of them and write their structures.
b. How will you prepare glycine by the Gabriel method?
- 26.15 Would you expect an α -amino acid to be more soluble or less in water at its iso-electric point than at higher or lower values?
- 26.16 Why should the iso-electric point for aspartic acid (2.98) be so much lower than that of leucine (5.98)?

Terpenes

Terpenes and terpenoids occur abundantly in nature in the leaves and fruits of many plants. The terpenes are the simple ten carbon atom containing compounds of the general formula $C_{10}H_{16}$. They are colorless liquids and are lighter than water. They are highly refractive and insoluble in water. They are responsible for the characteristic odor of many plants such as eucalyptus, citrus tree and pine needles. Their odor can be easily detected by crushing the leaves of a plant. Terpenes may be regarded as dimers of isoprene and the linking of two units of isoprene can give rise to three types of terpenes, as illustrated below:

a. *Acyclic*

Myrcene

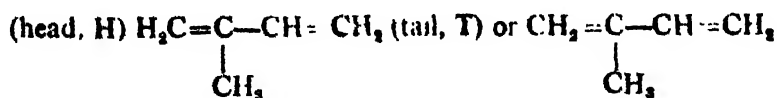
b. *monocyclic*

Limonene

c. *bicyclic*

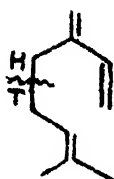
Sabinene

The term terpene usually is restricted to hydrocarbons but in practice it also applies to compounds containing oxygen as well, these include menthol, camphor, thymol, menthone, etc. The one common characteristic of all terpenes is that their carbon skeletons are eventually divisible into five carbon atom chains of isoprene and the two isoprene units are joined head to tail in a regular fashion in a terpene.

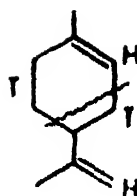


Isoprene (2-Methyl-
1,3-butadiene)

This structural correlation is known as the *isoprene rule*. This type of linking is shown for myrcene and limonene as follows:



Myrcene



Limonene

Terpenoids are also called *isoprenoids* because of the occurrence in their structures of the five carbon atom isoprene unit. The principal investigators in the field of terpenes were Wallach, Semmler, Baeyer and Tiemann.

27.1 OCCURRENCE OF TERPENES

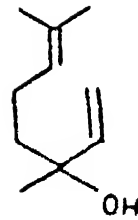
Fruits, leaves, seeds and flowers of almost all the plants possess characteristic odors. This odor (essence) is due to the presence of some steam volatile compounds known as *essential oils*. These oils are a mixture of many compounds but some of them are simple and consist mainly of one component. Essential oils are obtained by distilling the plant with water. The oil is then extracted from the distillate with an appropriate organic solvent and is purified by fractional distillation. Some essential oils with their terpenoid constituents are given below:

Source	Terpene	Structure
Rose	Geraniol	<chem>CC(=C)CC=CCO</chem>
Turpentine	α -Pinene	<chem>CC1=C(C2CC1)C=CC2</chem>
Caraway	Carvone	<chem>CC(=C)C1CC(=O)CC1</chem>

(Contd.)

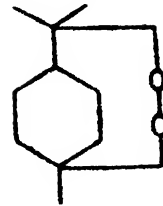
Coriander and
jesamine

Linalool



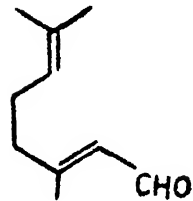
Eucalyptus

Cineole



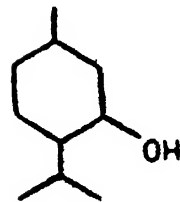
Lemon

Citral



Peppermint

Menthol



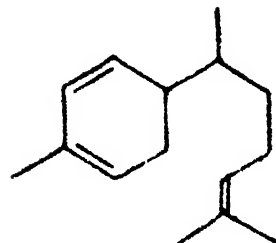
Cardamon

Terpineol



Ginger

Zingiberene



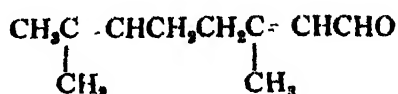
For many years, essential oils have been employed commercially in food flavoring, as medicinal agents and in perfumes.

27.2 CLASSIFICATION OF TERPENES

Terpenes and the higher members (terpenoids) are classified according to the number of isoprene units.

(i) Terpene—2 isoprene units ($C_{10}H_{16}$)

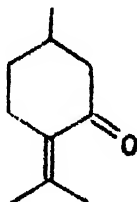
Citral



Limonene

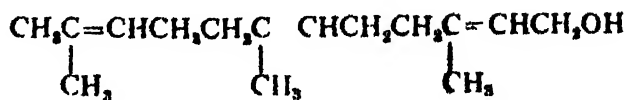


Pulegone

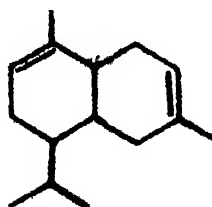
 α -Pinene

(ii) Sesquiterpene—3 isoprene units ($C_{15}H_{24}$)

Farnesol

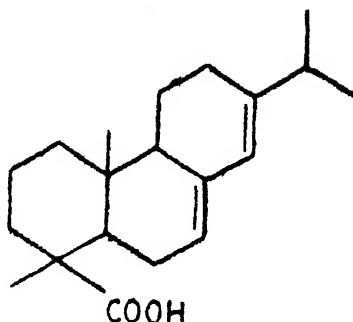


Cadinene

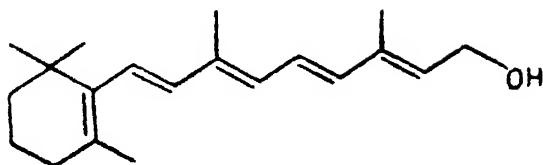


(iii) *Diterpene*—4 isoprene units ($C_{20}H_{32}$)

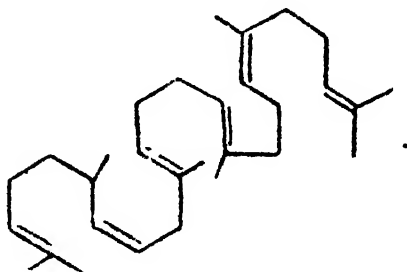
Abietic acid



Vitamin A

(iv) *Triterpene*—6 isoprene units ($C_{30}H_{48}$)

Squalene

(v) *Tetraterpene*—8 isoprene units ($C_{40}H_{64}$)

Lycopene—a red pigment obtained from ripe tomatoes.

(vi) *Polyterpene*— n isoprene units (C_5H_8) $_n$

Rubber—both natural and synthetic.

27.3 CITRAL

The main source of citral is lemon grass oil which contains this terpene to the extent of 60-80%. The oil is fractionally distilled and citral is obtained as a pale yellow oil with the odor of lemon. It may further be purified by making the sod. bisulfite adduct and then decomposing it with sod. carbonate solution. Citral is an open-chain terpene, which when heated with acid, undergoes ring-closure to give *p*-cymene.

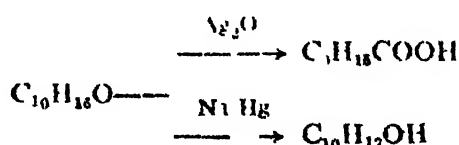
27.3.1 Constitution

1. The molecular formula of citral is found to be $C_{10}H_{16}O$
2. Citral adds two molecules of bromine.

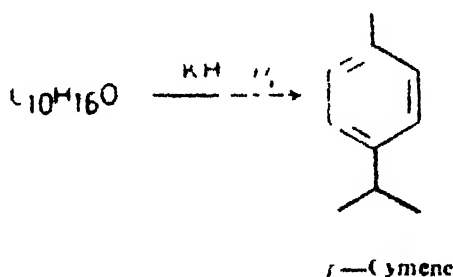


This shows that citral is doubly unsaturated.

3. Citral forms an oxime and reduces Fehling solution, which indicates the presence of an aldehyde group. This is confirmed by its oxidation and reduction reactions. On oxidation, citral yields an acid (geranic acid), while on reduction an alcohol (geraniol) is obtained

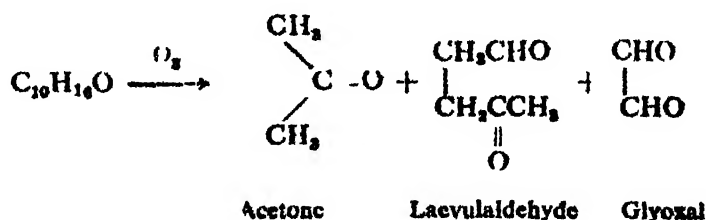


4. Heating citral with $KHSO_4$ or an acid, yields *p*-cymene, an aromatic compound. The molecular formula of citral is $C_{10}H_{16}O$, it contains two double bonds and an aldehyde group. The molecular formula for the

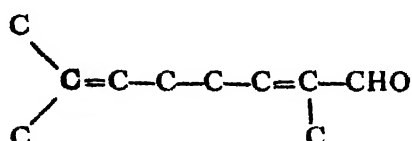


saturated compound obtained on reduction of citral is expected to be $C_{10}H_{22}$. Since this corresponds to the general molecular formula C_nH_{2n+2} for acyclic compounds, citral must also be an acyclic compound.

5. A clue to the structure of citral is obtained on ozonolysis of citral which gives a mixture of three products.

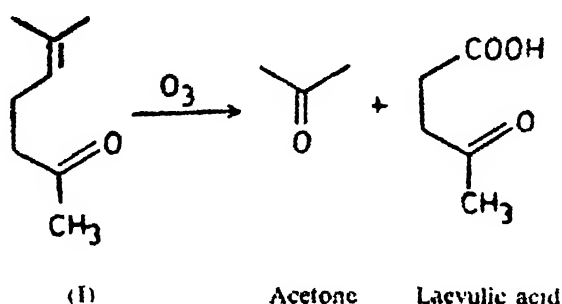


On the basis of these products, the carbon skeleton of citral can be assembled as follows:

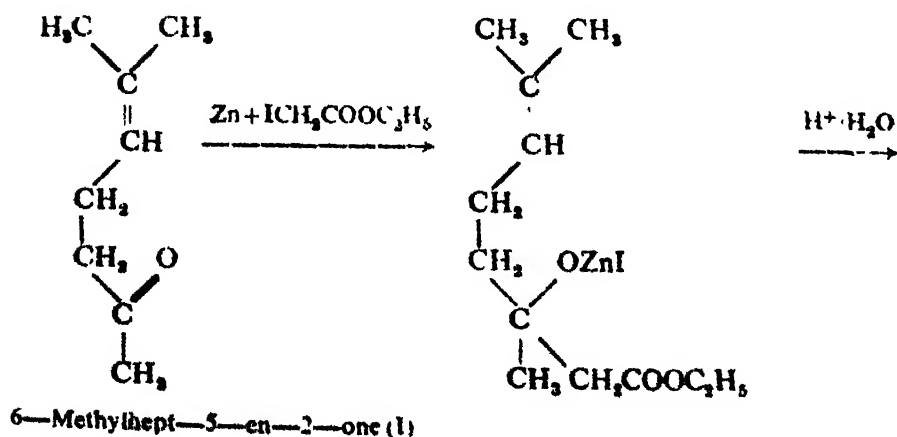


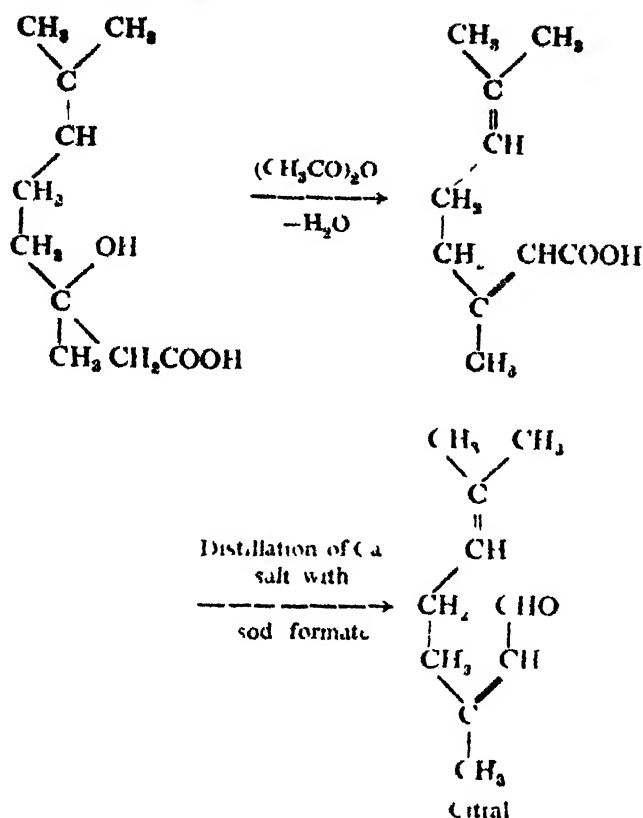
Putting the required hydrogen atoms gives the structure of citral.

6. The above structure for citral was proved by its treatment with aqueous K_2CO_3 and its conversion to acetaldehyde and an unsaturated ketone which was identified to be 6-methylhept-5-en-2-one(I). Its molecular formula was found to be $\text{C}_8\text{H}_{14}\text{O}$ and it added one mole of bromine. On ozonolysis this ketone gave acetone and laevulic acid.



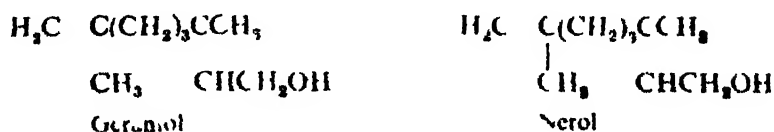
7. This structure of citral is supported by its independent synthesis.



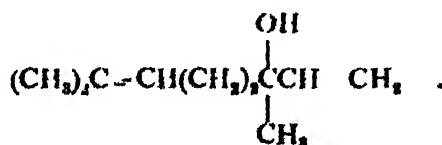


27.4 GERANIOL

Geraniol is an acyclic unsaturated primary alcohol and is the main constituent of geranium, rose, lemon and palmarose oils. Geraniol has the *cis*-configuration while its stereomer, nerol, is *trans*.



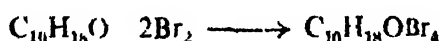
Geraniol, on reaction with dil. H_2SO_4 yields terpin hydrate, but with dil. phosphoric acid, dipentene is formed. On heating under pressure at 200° , geraniol is partially isomerized to a *tert* alcohol, linalool.



Geraniol is largely used in perfumery. It was first isolated from palmarose oil and has been found in numerous other essential oils. Geraniol esters such as geraniol formate, acetate, propionate, butyrate, etc., are used in perfumes, when a rose note is required predominantly in perfume or as a subsidiary modifier. The alcohol nerol which occurs in the essential oil of neroli, bergamot and others is also rose scented and is prized highly in the perfume industry.

27.4.1 Constitution

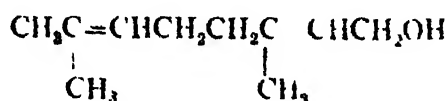
1. The molecular formula of geraniol is found to be $C_{10}H_{18}O$.
2. Geraniol adds two moles of bromine which shows that it contains two double bonds



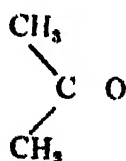
3. Oxidation of Geraniol with chromic acid yields a ten carbon aldehyde with the loss of a molecule of water



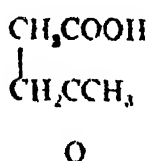
This indicates that geraniol is a primary alcohol. The first oxidation product, $C_{10}H_{16}O$, has been identified as citral and geraniol can be obtained from it by reduction. Geraniol therefore, must be the corresponding alcohol of citral. The carbon skeleton in geraniol is thus identical to citral. Hence the structure of geraniol must be formulated as follows:



4. This structure is further supported by its oxidative cleavage with aq. KMnO_4 which yields a mixture of the following three products, as well as by its synthesis

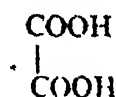


Acetone

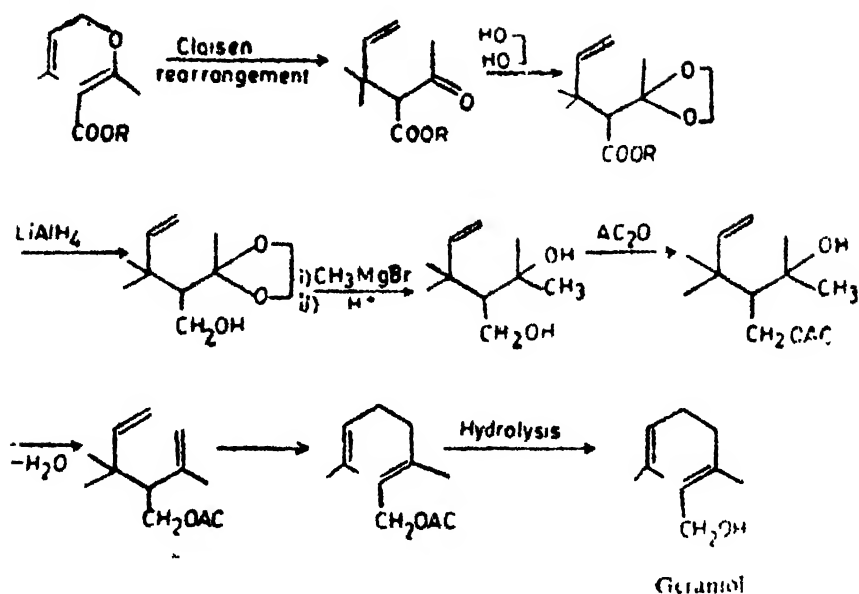


Laevulinic acid

and



Oxalic acid

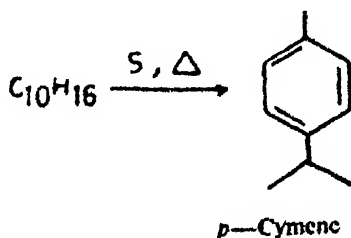
Synthesis:**27.5 LIMONENE**

Limonene is a monocyclic terpene and is widely distributed in plants oranges, lemon, citron, caraway and bergamot. It is a liquid which boils at 117° and is optically active. It also oxidizes fairly readily on exposure to air. A large amount of limonene is produced as a by-product in citrus fruit industry and is widely used in the perfume industry.

27.5.1 Constitution

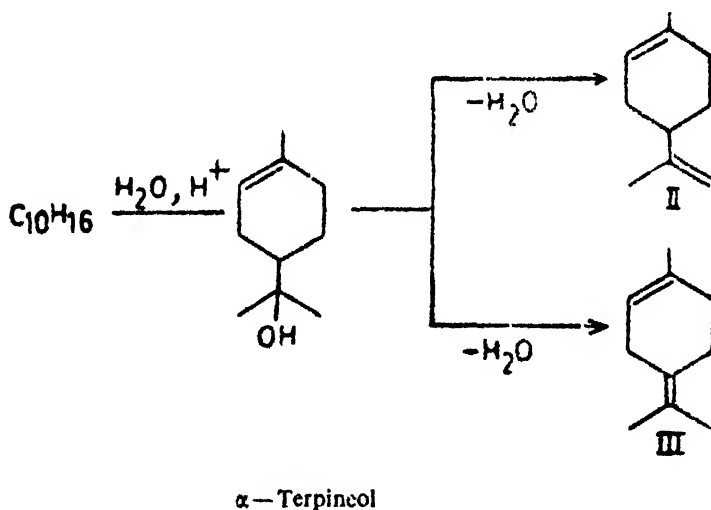
The constitution of limonene is based on the following information:

1. Its molecular formula, from analytical data, is found to be $C_{10}H_{16}$.
2. The unsaturation in limonene is indicated by the formation of a tetrabromo derivative with two moles of bromine and the production of *p*-menthane on catalytic hydrogenation. These reactions also demonstrate the presence of two double bonds in limonene.
3. Dehydrogenation of limonene with sulphur (or selenium) results in *p*-cymene.

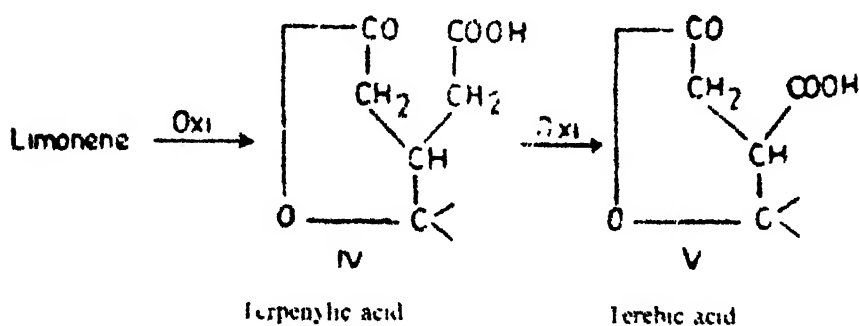


Thus limonene contains a cyclic, six-membered carbon skeleton.

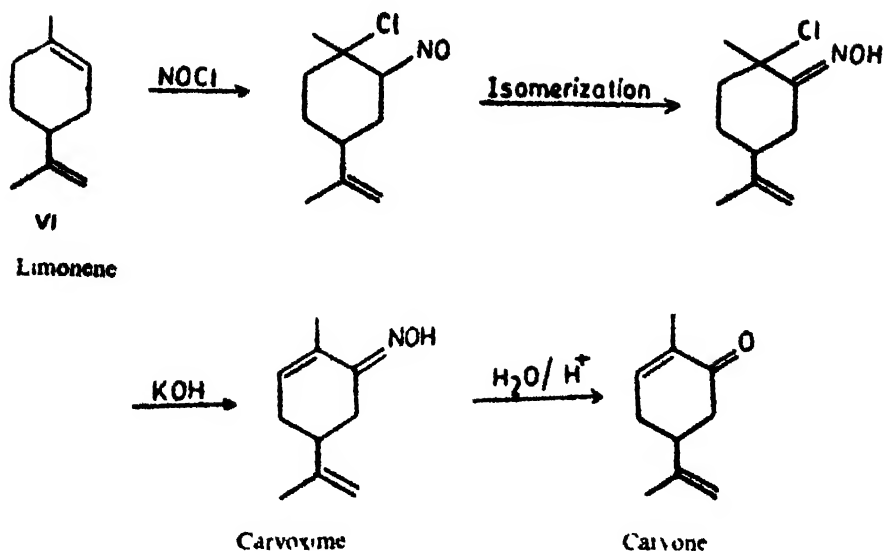
4. The position of the endocyclic ethylene linkage was based on the structure of α -terpineol. Limonene can be readily hydrated in the presence of a dil. mineral acid to α -terpineol. The latter, on dehydration can lead



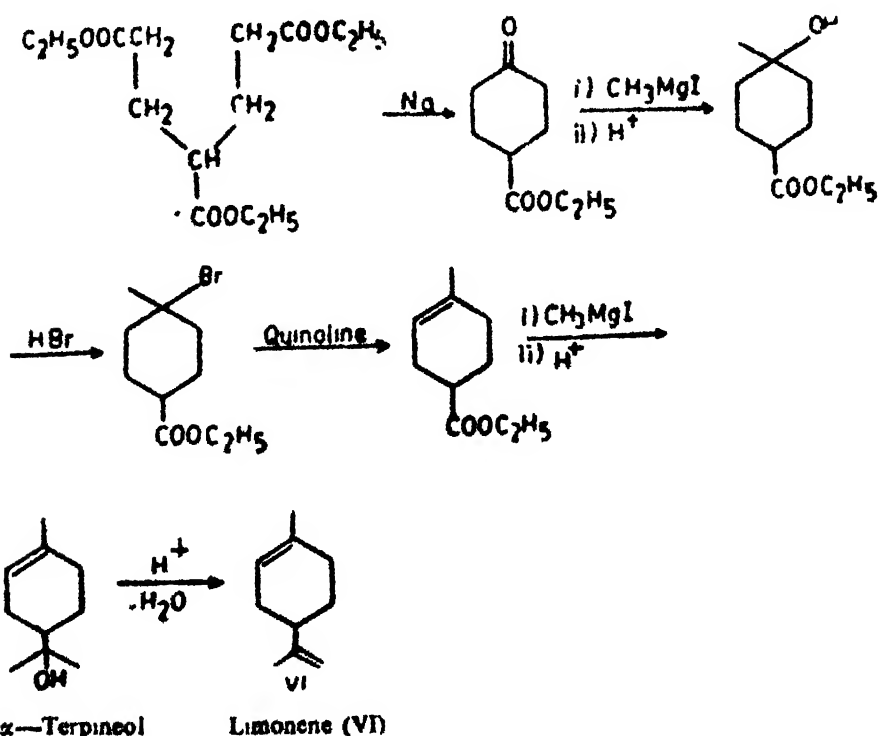
to two products (II, III). Since both these products contain an endocyclic double bond, therefore, it can be inferred that limonene also contains an endocyclic double bond. This has been established by the oxidation of limonene which gives terpenylic acid (IV) which on subsequent oxidation yields terebic acid (V).



5. The position of the second olefinic linkage is based on the structure of carvone. Limonene adds nitrosyl chloride (NOCl) which on treatment with KOH yields nitroso-limonene (carvoxime) and finally on acid hydrolysis results in carvone. On this basis, the structure of limonene can be formulated as (VI) and the above sequence of reactions can be written as follows:



6. This structure has been confirmed by an ingenious synthesis of limonene

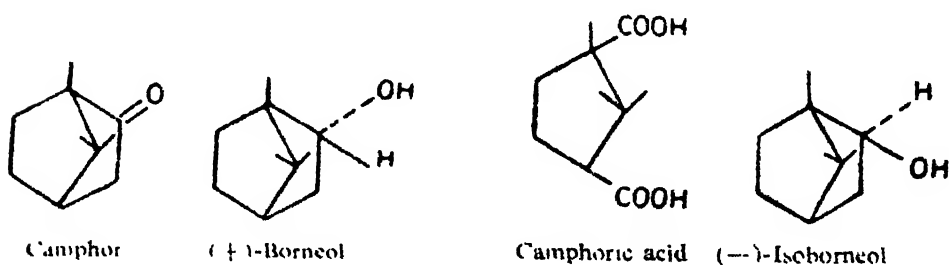


27.6 CAMPHOR

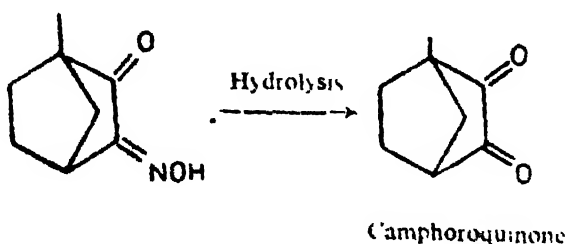
Camphor is a bicyclic ketone, its principal natural source being *Cinnamomum Camphora* (Camphor tree). It is a colorless crystalline solid, m.p. 179°

Camphor is optically active and both the forms occur naturally. The (+)-form is extracted by steam distillation of wood chips of *laurus camphora*, a tree found in Japan and China. The (-)-form occurs in certain essential oils, i.e., in the *artemisia austrachanica*. Camphor is used in medicines, for making smokeless powder and as a plasticizer for cellulose nitrate in the manufacture of celluloid. A common use of camphor is as a solvent in the Rast's method for the determination of molecular weight by depression of melting point.

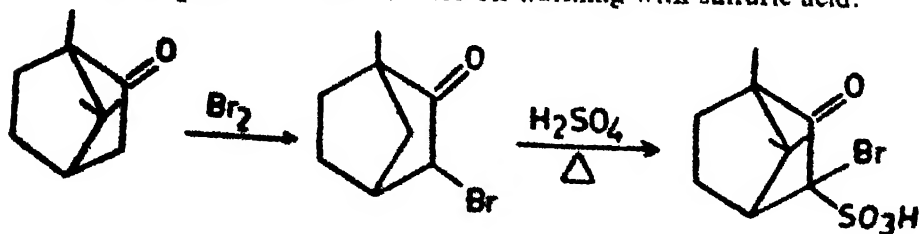
Most of the chemical reactions of camphor are characteristic of the keto-group. This group reacts with the usual reagents like phenylhydrazine, hydroxylamine, sod. bisulfite, etc. On reduction it yields a secondary alcohol and this introduces a third asymmetric center into the molecule. Thus two epimeric alcohols are obtained on reduction of (+)-camphor. Oxidation with nitric acid results in the formation of camphoric acid. Camphor possesses a reactive methylene group adjacent to the carbonyl group and thus forms



is nitrosocamphor on reaction with HNO_2 or isopentyl nitrite, which on hydrolysis forms camphoroquinone



Bromination of camphor yields 3-bromocamphor which is converted into 3-bromocamphor-3-sulfonic acid on warming with sulfuric acid.

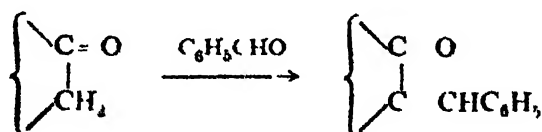


27.6.1 Constitution

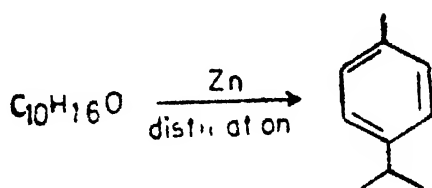
1. The molecular formula of camphor is $C_{10}H_{16}O$.

2. Camphor forms addition compounds with hydroxylamine, semicarbazide and sod. bisulfite, and on oxidation with nitric acid leads to a dicarboxylic acid. Therefore, the oxygen atom is present as a keto group.

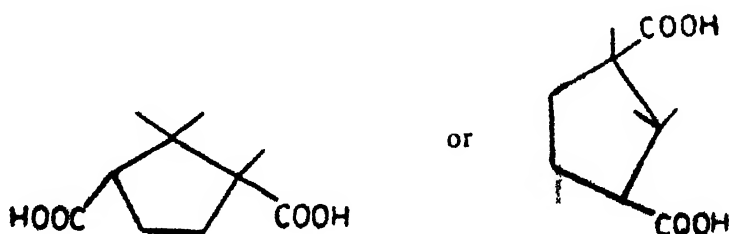
3. Camphor condenses with benzaldehyde to form a monobenzilidene derivative. This suggests the presence of a $-\text{CO}-\text{CH}_2-$ grouping. This is further confirmed by the formation of isonitrosocamphor with nitrous acid.



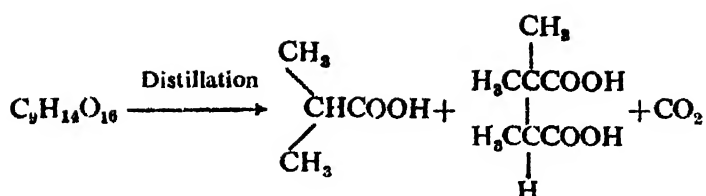
4. On distilling camphor with zinc dust *p*-cymene is obtained. It indicates that camphor contains one six-membered ring



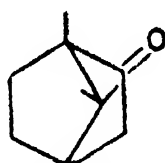
5. A clue to the structure of camphor comes from the identification of its degradation products. On oxidation with nitric acid, camphor forms camphoric acid ($C_{10}H_{16}O_4$) and subsequently camphoronic acid ($C_9H_{14}O_4$). Camphoric acid ($C_{10}H_{16}O_4$) is a saturated dicarboxylic acid. It forms a monoester easily but a diester with great difficulty. Its structure has been postulated to be the following.



Camphoronic acid is an acyclic acid in which the three carboxyl groups are attached to different carbon atoms as it is not easily decarboxylated. On distillation at atmospheric pressure it yields isobutyric acid, trimethylsuccinic acid and carbon dioxide is evolved.

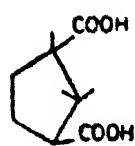
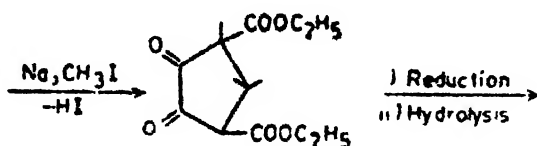
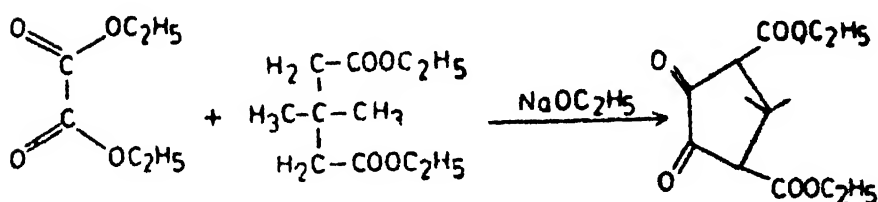


Now since camphor has a $-\text{CO}-\text{CH}_2-$ grouping its structure may be written as follows:

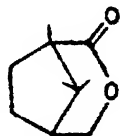
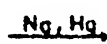
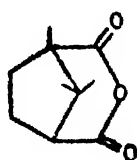
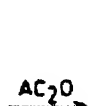


Camphor

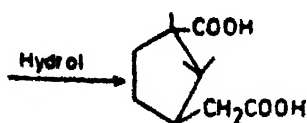
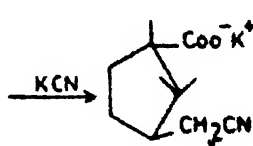
6. The structure has been confirmed by its independent synthesis.



Camphoric acid



Camphoric acid



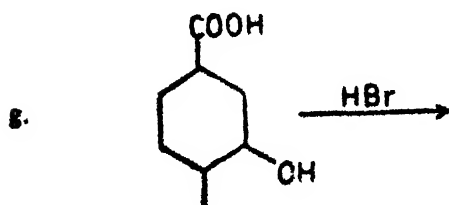
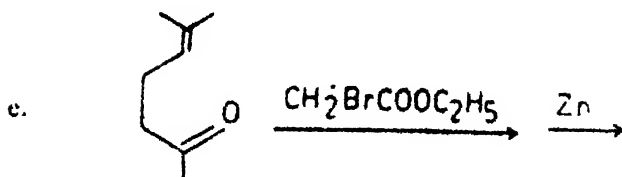
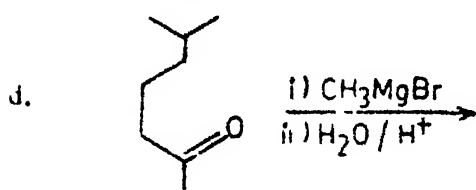
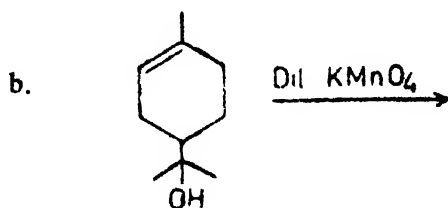
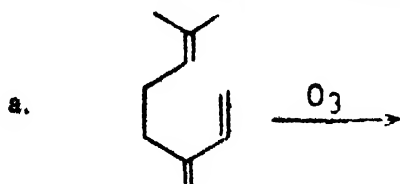
Homocamphoronic acid



Camphor

QUESTIONS

27.1 Predict the products of the following reactions :

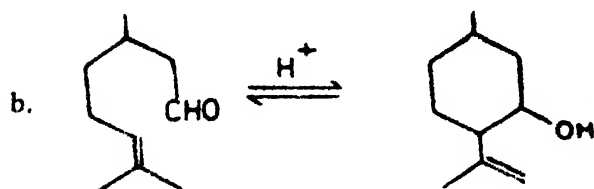
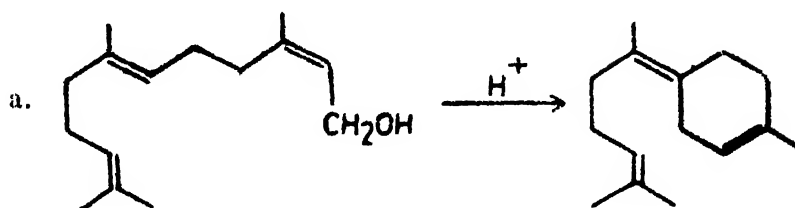


27.2 How are terpenes classified? Give examples.

27.3 Discuss the structure of limonene.

27.4 What are essential oils? Describe their uses?

27.5 Suggest a mechanism for each of the following reactions:



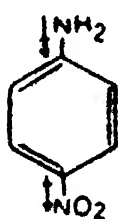
27.6 What are the important sources of geraniol? Discuss its structure. How has it been synthesized?

27.7 How will you prove that camphor is a saturated cyclic ketone containing a $-\text{CH}_2-\text{CO}-$ group?

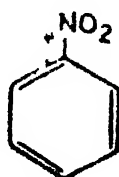
Answers to Questions

CHAPTER 1

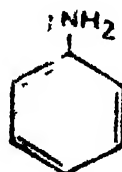
1.1 See the text 1.2 See Sec. 1.5 1.3 See Sec. 1.5 1.4 In *cis*-diol the hydroxyl groups are close together while in the *trans*-isomer they are too far apart, the former structure thus can form hydrogen-bond. 1.5 Due to intramolecular hydrogen-bonding in *o*-nitrophenol, the intermolecular association is reduced, this makes it more volatile. Conversely because of intramolecular hydrogen-bonding, *o*-nitrophenol is incapable of forming hydrogen-bond with water and is thus less soluble in water compared to the other isomers. 1.6 See Sec. 1.5 1.7 (a) The direction of dipole moments in these compounds is as follows,



1.53 D



3.95 D



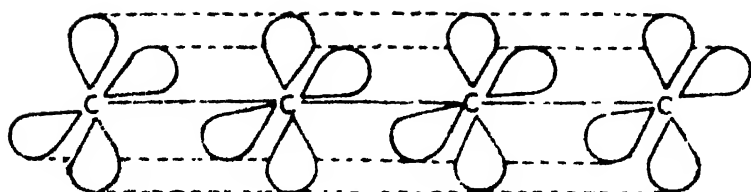
6.10 D

The values for the first two compounds show that NH_2 and NO_2 groups induce dipole moments in opposite directions with respect to benzene. In *p*-nitroaniline the dipole moments of these groups reinforce each other to increase the net value.

(b) There is more charge separation in acetaldehyde because $\text{CH}_3-\overset{\text{H}}{\underset{\text{O}}{\text{C}}}=\text{O}$, contribution is greater than $\text{CH}_3-\overset{+}{\text{C}}\text{H}-\text{CH}_2^-$.

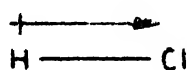
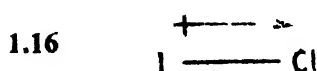
(c) Nitrobenzene would have a larger value than nitromethane because of a greater distance of charge separation 1.8 H_2SO_4 ($\text{S} = 0$, $\text{O} = -0$), CO_2 ($\text{C} = 0$, $\text{O} = -0$), HCO_2^- ($\text{C} = 0$, $\text{O} = -1$).

1.9 NH_3 , CH_3OCH_3 , $\text{C}_6\text{H}_5\text{NH}_2$ and ICl will have a permanent dipole moment. 1.10 Because of the following orbital overlap.



This causes the central C—C bond to be shortened. 1.11 C—H, C—C and C—Cl bonds are sp^3 hybridized, therefore, they would be longer than C=C and C≡C bonds.

1.12 See the text 1.13 $C_6H_5NH_2$ and CH_3OH possess dipole moment while CCl_4 and *trans* 2-butene do not. 1.14 See Sec. 1.5 1.15 C_2H_4 contains a C=C double bond in which a carbon atom is bonded to only three other atoms.



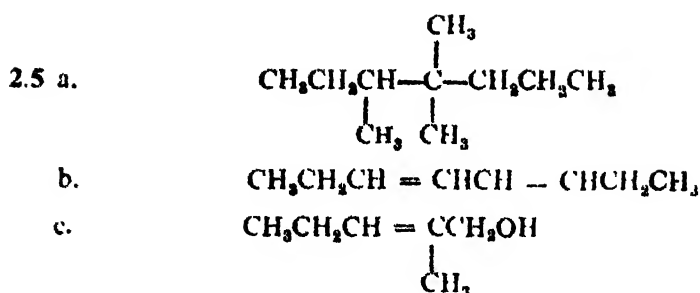
1.18 Linear, tetrahedral, tetrahedral, trigonal planar, tetrahedral, trigonal planar.

1.19 See the text, 1.20 Carbon, 180° .

1.21 The hydrogen—bonds formed between water molecules hold them in an "open network" structure in the ice crystal. As the ice melts, hydrogen—bonds are broken and the resulting liquid occupies less space than the original solid.

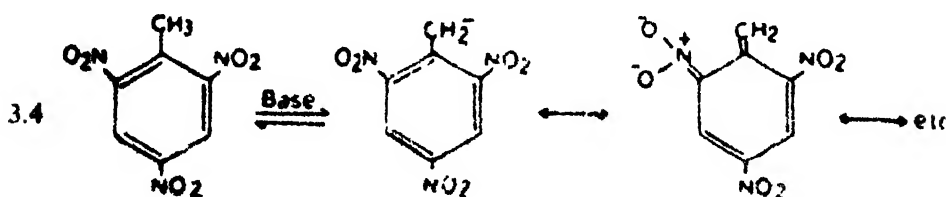
CHAPTER 2

- 2.1 (a) Hex-1-en-5-yne (b) 3-Cyclopentyl-2, 4-dimethylpentane (c) 1, 4-Cyclohexadiene (d) Cyclopent-1, 3-dione (e) N,N, 3-trimethylbutanamide (f) Ethanoyl chloride (g) 4, 6-Heptadien-2-yne (h) Propen-1-ol (i) 4-Penten-2-one (j) 1,2-Ethanediol (k) 2,3-Dichloro-3-methylbutanal (l) Methyl 3-aminopropanoate (m) *tetra*-Chloromethane (n) Ethyl-2-methyl-2-butenolate (o) 2, 3-Dichloro-1, 5-dipentanamide (p) 3-Bromo-1-propene (q) 5-Carbamoylhexanoyl chloride (r) Ethyl 2,2-dimethyl-4-oxobutanoate (s) 2-Methyl-4-oxobutenonitrile (t) 2-Formyl-2-methylcyclohexanone (u) 3-Chloroformylbutanoic acid 2.2 (a) 4-Penten-2-yne (b) 2-Ethyl-4-pentenal (c) 2-Chloro-1,3-butadiene (d) 3-Ethyl-5-methylheptane (e) 1-Butene (f) 3-Methyl-1-propyne (g) 1,3-Pentadiyne (h) 3-Butenoic acid (i) 7-Hydroxy-3-heptanone (j) Hex-4-en-1-ol (k) 1-Buten-3-yne (l) correct 2.3 See p. 17 2.4 See Sec. 2.1.1



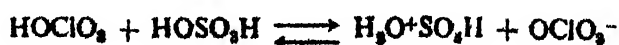
CHAPTER 3

3.1 (a) Yes, because the two β -Br groups are more effective in stabilizing the anion inductively (b) The trifluoromethyl group withdraws electrons inductively making the electron pair on the N-atom less available for donation 3.2 (a) NH_3 , CH_3CONH_2 , CH_3COOH , HCOOH , CCl_3COOH , CF_3COOH (b) NH_3 , OH^- , $(\text{CH}_3)_3\text{N}$, CH_3NH_2 , NH_3 , $\text{C}_6\text{H}_5\text{NH}_2$, CH_3OH 3.3 See the text.



The anion is stabilized by resonance with the $-\text{NO}_2$ groups.

3.5 See Sec. 3.1.3 3.6 $1\text{-Butene} + \text{H}_2 \xrightarrow{\text{Cat.}} \text{Butane} \quad 30.3 \text{ kcal/mole}$, $1,3\text{-Butadiene} + 2\text{H}_2 \xrightarrow{\text{Cat.}} \text{Butane} + 57.1 \text{ kcal/mole}$. 1,3-Butadiene might be expected to evolve twice the heat of 1-butene ($30.3 \times 2 = 60.6 \text{ kcal/mole}$), but it evolves only 57.1 kcal/mole. The difference ($60.6 - 57.1 = 3.5 \text{ kcal/mole}$) is the resonance energy (b) No, because 2-butene has a lower heat of hydrogenation (28 kcal/mole) due to its own stability. 3.7 Acids: BF_3 , NO_2^+ , Ag^+ , Bases: CH_3CN , H_2O , CH_3OH , Neither $\text{HC}\equiv\text{CH}$, C_6H_6 . IIF 3.8 See p. 46 3.9 *p*-Nitrophenol, phenol, *p*-cresol. $-\text{NO}_2$ group is electron-withdrawing whereas $-\text{CH}_3$ is electron-donating 3.10 See Sec. 3.3 (d) See Chapter 11 (b) The radical is stabilized by resonance (c) The charged structures absorb in the visible region. 3.11 Because of the presence of three fluorine groups, the release of proton is facilitated. 3.12 None of the pure acid is ionized. In the mixture, however, stronger HClO_4 donates a proton to H_2SO_4 .



3.13 (a) $\text{CH}_3\text{CH}_2\underset{\text{Cl}}{\text{CHCOOH}}$ is the strongest acid because the electron—with-

drawing Cl group is nearer to the carboxyl group (b) Propylamine

3.14 See the text.

3.15 $\text{C}_6\text{H}_5\text{COOH} + \text{H}_2\text{O} \rightleftharpoons \text{C}_6\text{H}_5\text{COO}^- + \text{H}_3\text{O}^+$

$$K_a = \frac{[\text{C}_6\text{H}_5\text{COO}^-][\text{H}_3\text{O}^+]}{[\text{C}_6\text{H}_5\text{COOH}]}$$

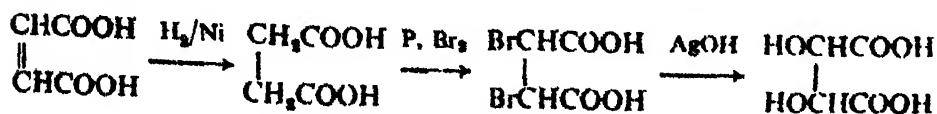
If the acid is half-ionized, then $[\text{C}_6\text{H}_5\text{COOH}] = [\text{C}_6\text{H}_5\text{COO}^-]$. In that case:

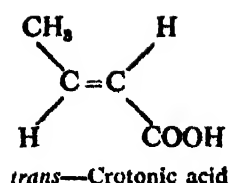
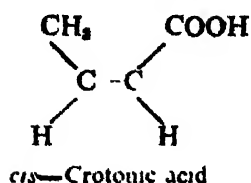
$$K_a = [\text{H}_3\text{O}^+] \text{ or } \text{pH} = \text{p}K_a$$

CHAPTER 4

4.1 See the text 4.2 a. See Sec. 4.2 b. No The compound will not show optical activity as it is internally compensated because both the carbon atoms carry identical groups. 4.3 a. Positional b. None c. None d. Positional e. None f. Functional g. Geometric 4.4 a. No. b. Yes c. Yes d. No (because the *trans* arrangement around the double bond would put the remaining carbon atoms too far apart to form a ring) e. Yes. 4.5 Butanone 4.6 a. R b. S c. S d. S e. R f. S 4.7 See p. 61 b(i) Enantiomers (ii) Enantiomers 4.8 a. 2 b. 4 c. 5 d. None e. 2 f. 2 g. 2 h. 2 4.9 a. true b. false d. false e. false f. true g. false h. true i. false 4.10 (R)-Methylpentanoic acid 4.11 See the text. 4.12 See the text. 4.13 See the text 4.14 See the text 4.15 A carbon atom linked to four different groups or atoms is referred to as asymmetric.

A molecule with an asymmetric carbon atom has stereoisomers which are known as enantiomers, i.e., they are optically active such as mandelic acid, $\text{C}_6\text{H}_5\text{CHOHCOOH}$. Several classes of compounds still show optical isomerism despite the fact that they do not contain an asymmetric carbon atom, for instance, the diphenyl derivatives, spiro compounds, etc. Therefore, the essential condition for a compound to exhibit optical isomerism is that the mirror images are non-superimposable, this is known as dissymmetry. 4.16 See Sec. 4.7. 4.17 (a) Yes, possible for instance, allenes and lactic acid.

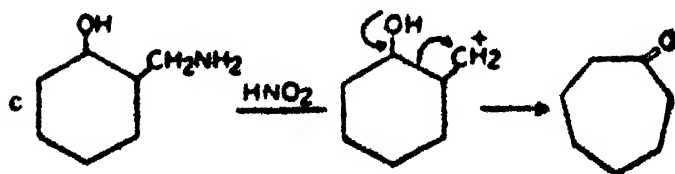
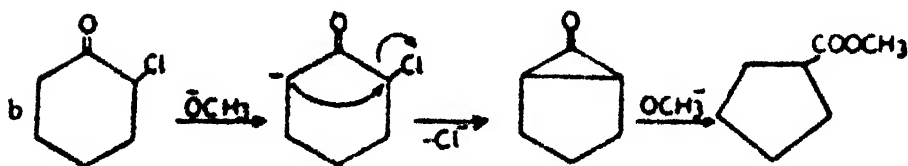
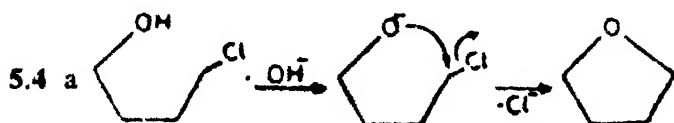


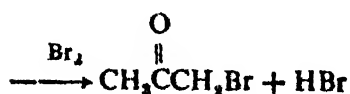
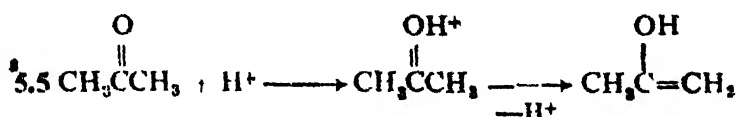
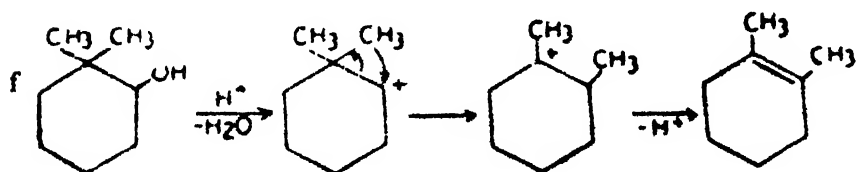
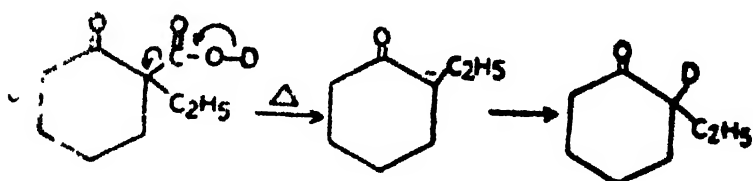
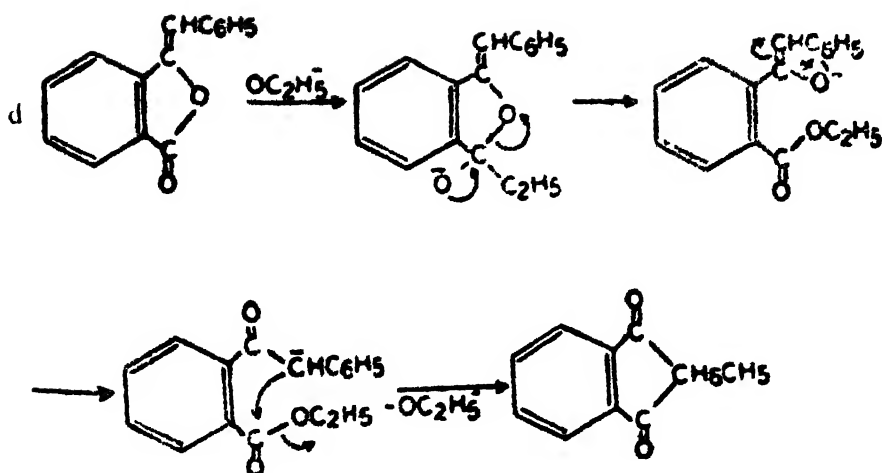


(b) The capital letters D and L refer to configuration and hence no relationship with the sign of rotation (c) A *meso* form has a net rotation of zero. i.e. optically inactive and is a diastereomer of each of the enantiomeric form of the compound. It cannot be resolved into its optically active components. A *racemic* form also shows an overall rotation of zero but it can be separated into its optical enantiomers. 4.18 See Sec. 4.4 (method 2) 4.19 See the text. 4.20 (a) See Sec. 4.7 (b) Enantiomers possess identical melting points, physical and chemical properties. Both contain an asymmetric carbon atom. They differ because the optical rotation is equal and opposite. 4.21 See Sec. 4.6.2, 4.22 $\text{CH}_3\text{CHOHCOOH}$.

CHAPTER 5

5.1 See the text 5.2 See Sec. 5.5.3 5.3 Species A, B and C can be stabilized by resonance





5.6 $(\text{CF}_3)_3\text{C}^+$, $(\text{CCl}_3)_3\text{C}^+$, $(\text{CH}_3)_3\text{C}^-$, $(\text{CH}_3)_3\text{C}_6\text{H}_5\text{C}^+$, $(\text{C}_6\text{H}_5)_3\text{C}^+$.

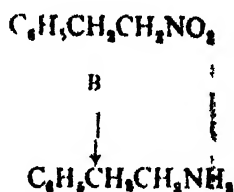
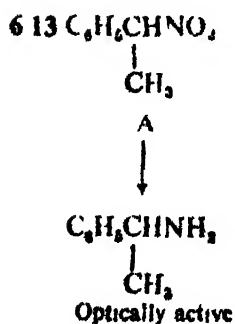
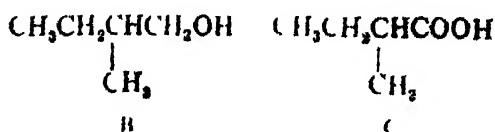
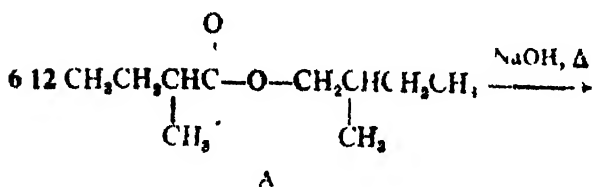
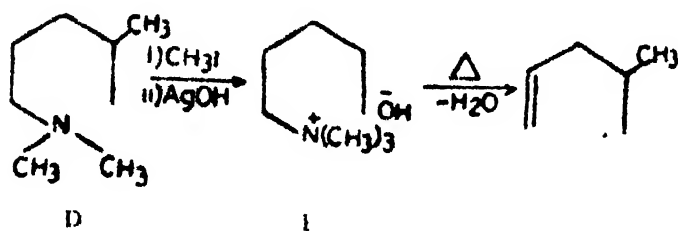
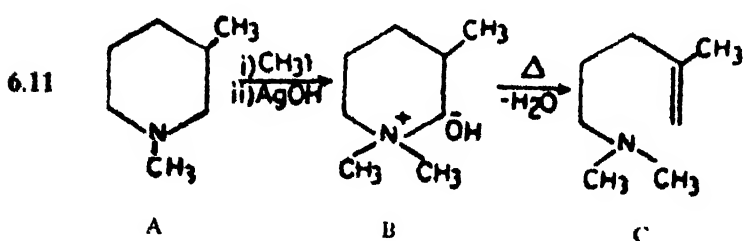
5.7 Electrophiles: SO_3 , NO_2^+ , H_3O^+ , Br^+

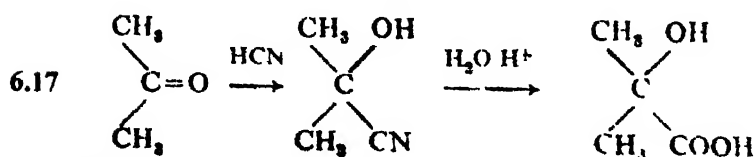
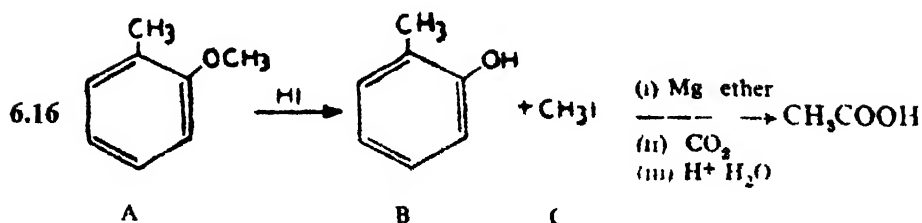
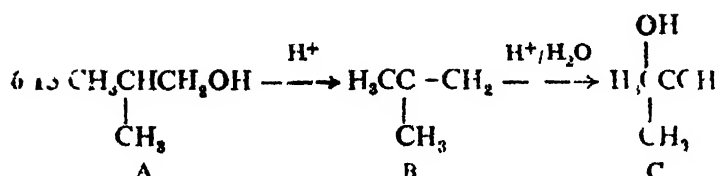
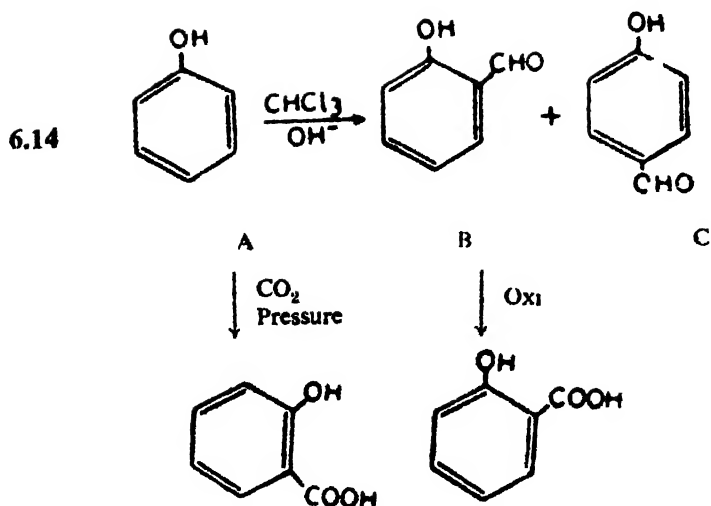
Nucleophiles: CH_3OH , RS^- , NH_3 , OH^-

CHAPTER 6

6.1 See Sec. 6.4/2 6.2 (a) See the text (b) No, it can be an azeotropic mixture. 6.3 See the text 6.4 Since the solvent system initially employed is non-polar and non-polar compounds are adsorbed only weakly on alumina, we

expect the least polar compound to be eluted first, i.e. anthracene, *p*-cresol can form hydrogen-bond with the hydroxyl groups on alumina surface so it is strongly adsorbed and will be eluted last. Chlorobenzene is also polar but shows intermediate elution 6.5 $C_4H_5N_2O$ 6.6 122, $C_7H_6O_4$ 6.7 C_8H_8O 6.8 $C_7H_6O_2$ 6.9 $C_4H_6O_4$ 6.10 C_8H_7N





D is obtained by hydrolysis, therefore, C, would be



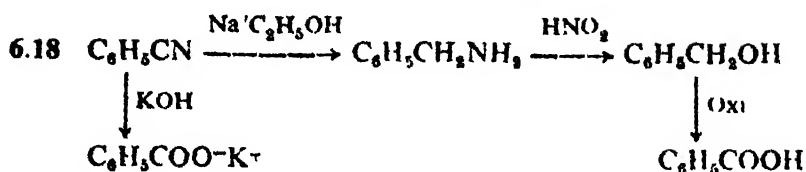
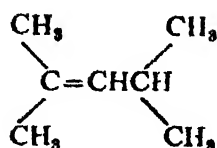
C is obtained from B by reacting with bromine and phosphorus, hence B is



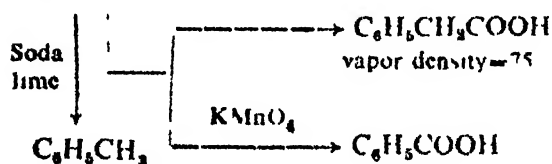
The aldehyde is thus



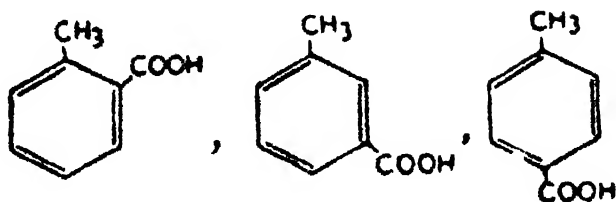
and the alkene (A) is



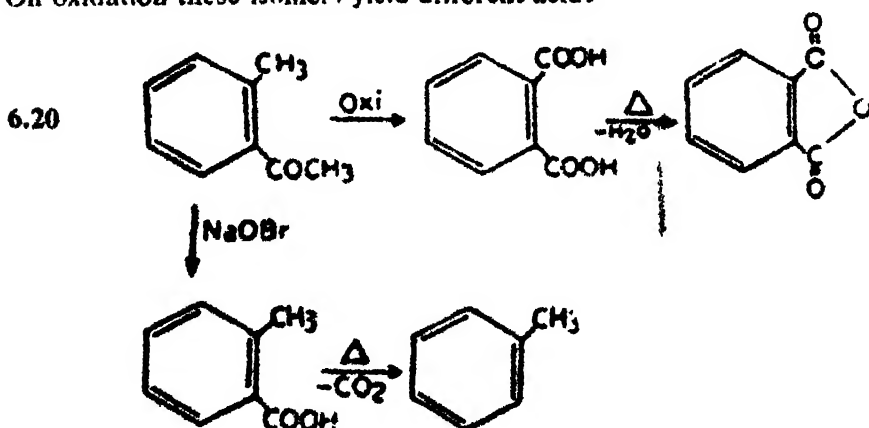
A

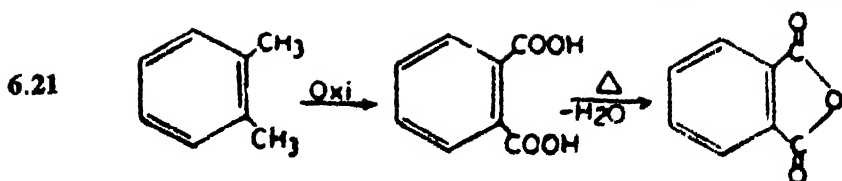


Isomers:

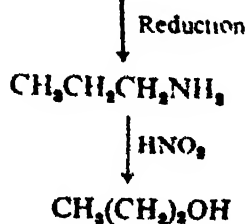
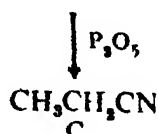
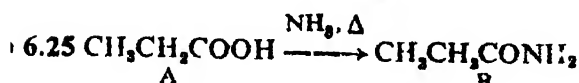
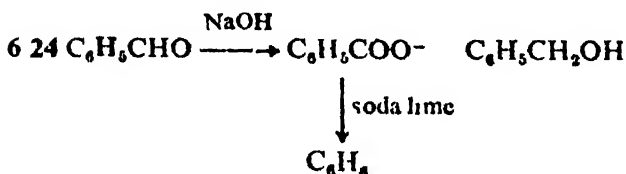
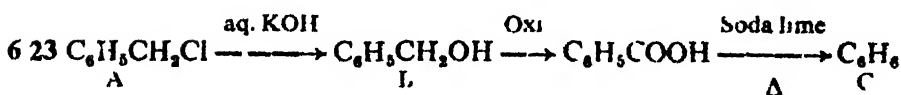
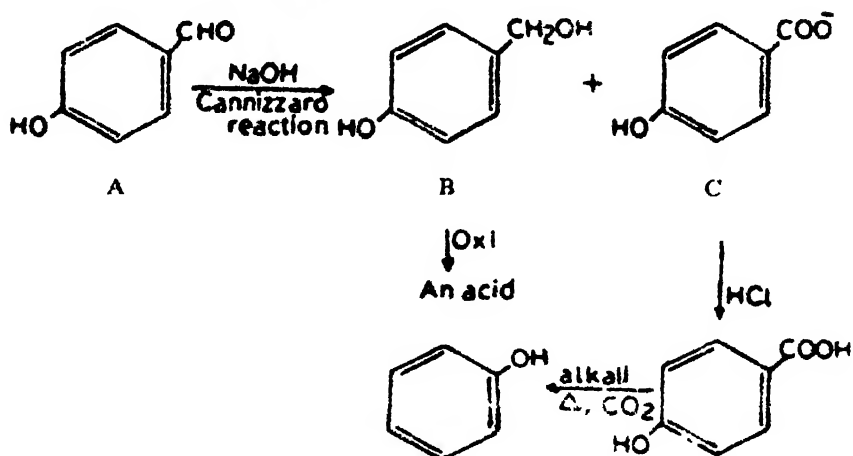


On oxidation these isomers yield different acids

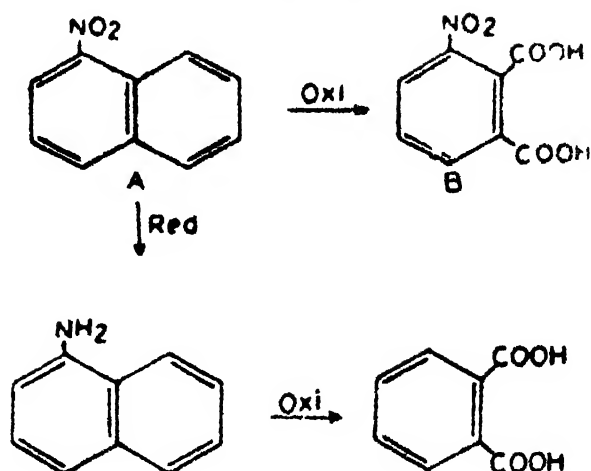




6.22 Molecular formula $\text{C}_7\text{H}_6\text{O}_2$



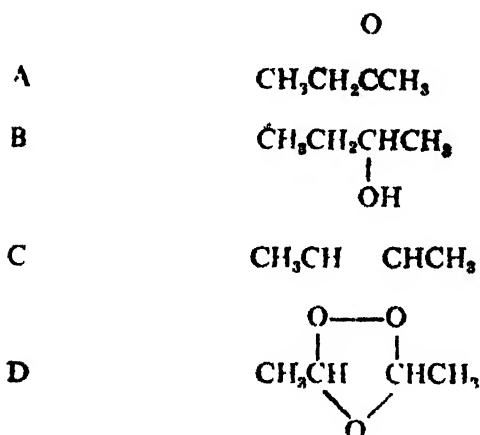
6.26 Molecular formula of A is $C_{10}H_7NO_2$



6.27 Succinic anhydride

6.28 Since the ketone undergoes haloform reaction it should contain the

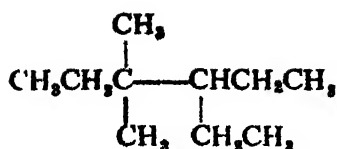
grouping $\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{CH}_3 \end{array}$. Formation of CH_3CHO on ozonolysis suggests that the alkene is symmetrical. Therefore, the compounds have the following structures



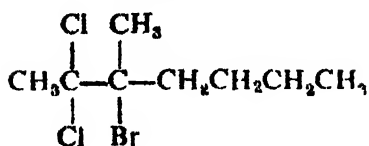
CHAPTER 7

7.1 Cracking is concerned with the breaking of the high boiling petroleum fraction into smaller fragments by heating and in the presence of a catalyst. The unreactive alkanes break into three and four carbon alkanes. 7.2 Five

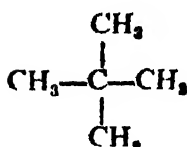
7.3 a.



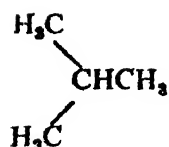
b.



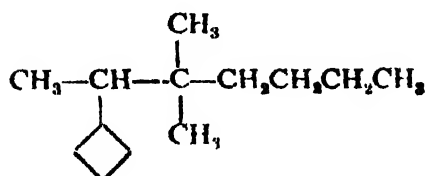
c.



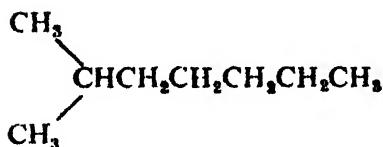
d.



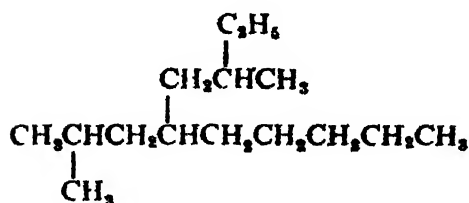
e.



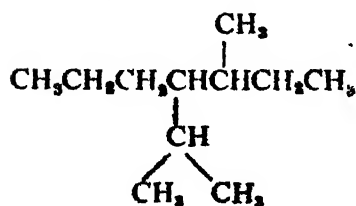
f.



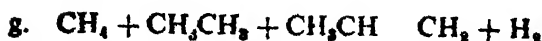
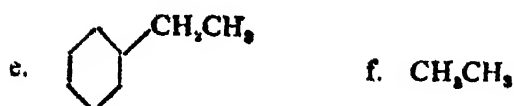
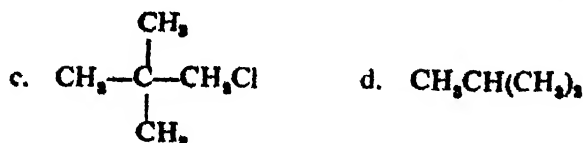
g.



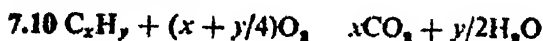
h.



7.4 Neo Pentane 7.5 An octane number of 85 means that the *iso*-octane: octane mixture contains 85% of *iso*-octane. 7.6 (a) The latter compound has a larger surface area (b) Because it is more stable (c) Forms H-bond with water (d) It is incapable of being fragmented into smaller fragments (e) It functions as an anti-knock. 7.7 See the text



7.9 See the text



$$\text{CO}_2 = 2.2 \text{ g}$$

$$\text{weight of carbon} = \frac{2.2}{44} \times 12 = 0.6 \text{ g}$$

$$\text{weight of water} = 1.8 \text{ g}$$

$$\text{weight of H} = \frac{1.0}{18} \times 2 = 0.2 \text{ g}$$

$$\text{Atomic ratio : C : H} = \frac{0.6}{12} : \frac{0.2}{1} = 1 : 4$$

Therefore, empirical formula is CH_4

$$\text{Weight of the hydrocarbon : } 0.6 + 0.2 = 0.8 \text{ g}$$

$$\text{In } 22.4 \text{ l (1 molar volume) the hydrocarbon is } \frac{0.8}{16} \times 22.4 = 1.12 \text{ moles}$$

$$\text{Weight of 1 mole} = 16 \text{ g}$$

Molecular formula is CH_4

$$\text{Moles of oxygen required for C} = \frac{0.6}{12} \text{ and for H} = \frac{0.2}{2}$$

$$\text{Total oxygen required} = 0.05 + 0.05 = 0.1 \text{ mole}$$

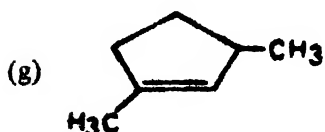
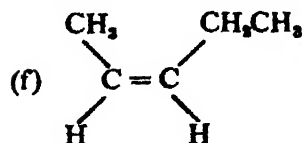
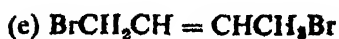
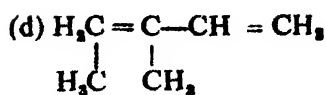
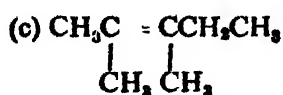
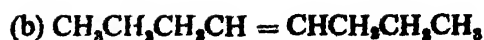
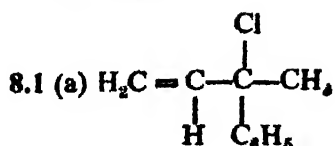
7.11 See Sec. 7.6 3 and 7.8 7.12 See the text.



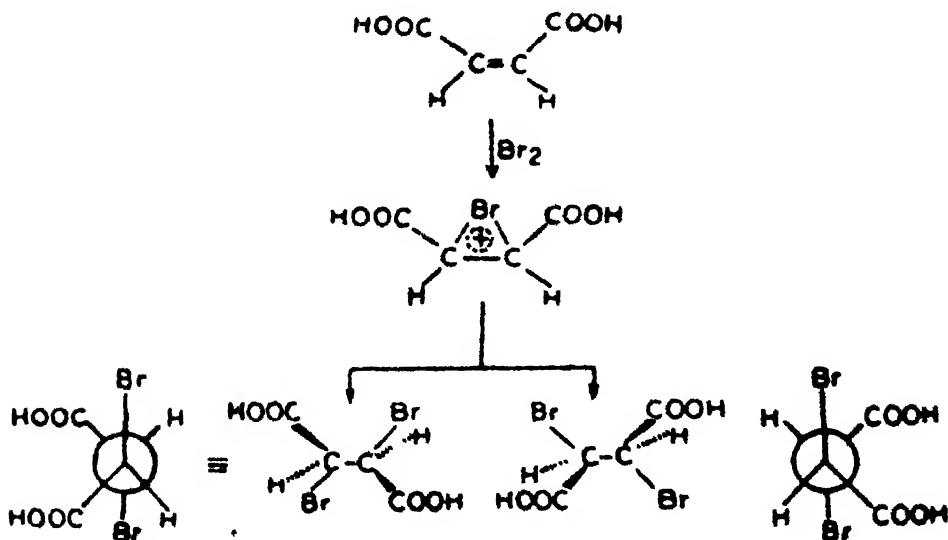
7.14 See the text 7.15 Grignard reaction, hydrogenolysis and reduction

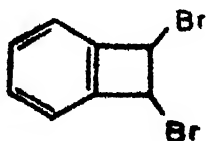


CHAPTER 8

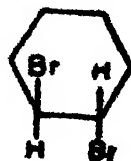


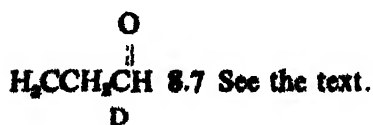
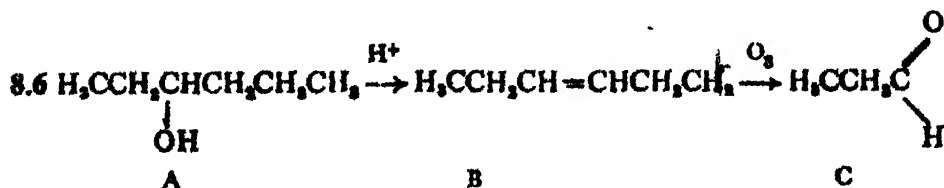
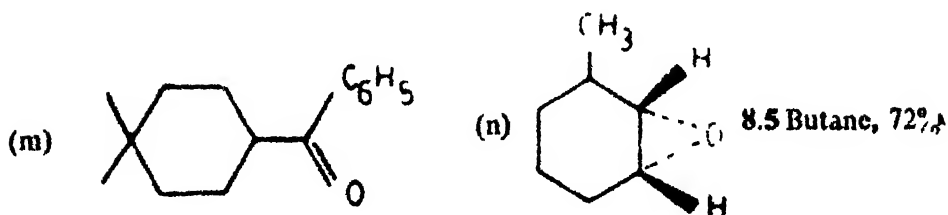
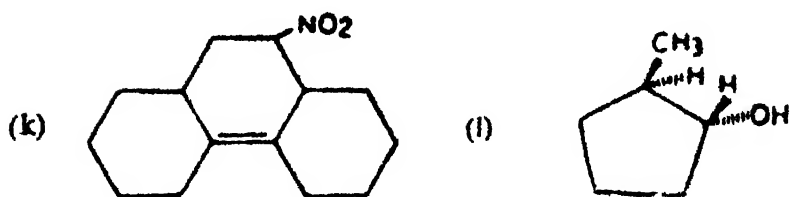
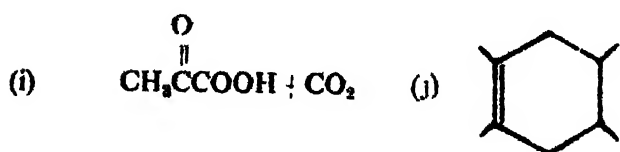
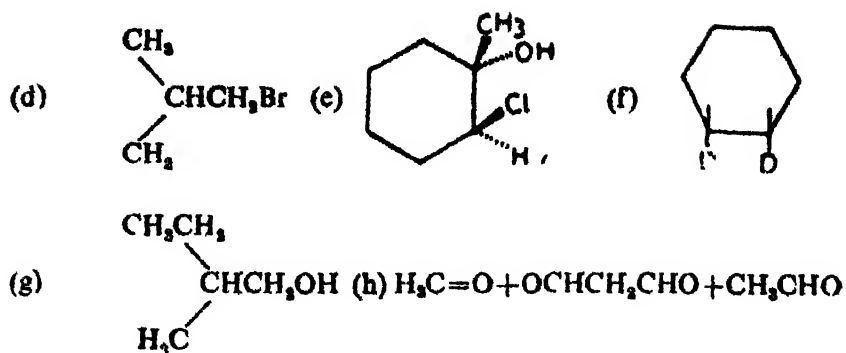
8.2 See the text 8.3 Addition of bromine

 to maleic acid takes place in a *trans* manner.

 When bromine is added to fumaric acid instead it is found that the two products are identical, i.e. a *meso* form is obtained. 8.4 (a) $\text{BrCH}_2\text{CH}_2\text{Br}$

 and $\text{H}_3\text{COCH}_2\text{CH}_2\text{Br}$ (b)


(c)





8.8 See Sec. 8.5 8.9, 8.10 See the text 8.11 (a) $\text{CNCH}=\text{CH}_2$ (b) $\text{CH}_3\text{CH}=\text{CH}_2$ (c) $\text{H}_3\text{COCOOCH}_2\text{C}=\text{CH}_2$ (d) CH_3CHCl_2 8.12 See Sec. 8.7.1 8.13 See



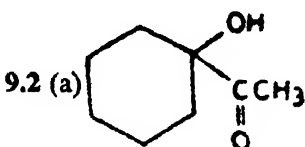
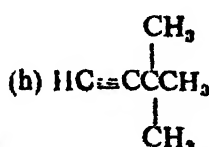
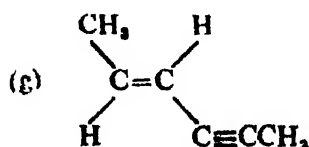
the text 8.14 See Sec. 8.4 8.15 See the text 8.16 a weak acid 8.17 See the text 8.18 See p. 141 8.19 See Sec. 8.5.

CHAPTER 9

9.1 (a) $\text{HOCH}_2\text{C}\equiv\text{CCH}_2\text{OH}$ (b) $\text{H}_3\text{C}-\text{CHC}\equiv\text{CH}$ (c) $\text{ClCH}_2\text{C}\equiv\text{CCH}_2\text{Cl}$
(d) $\text{BrC}\equiv\text{CCHCH}_2\text{CH}_3$ (e) $\text{CH}_3\text{C}\equiv\text{C}-\text{Na}^+$

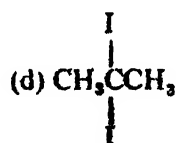


(f) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{C}\equiv\text{CCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$

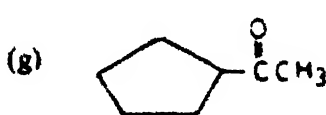
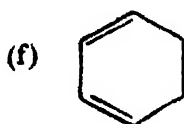


(b) $\text{CH}_3\text{COOH} + \text{HCOOH}$

(c) no reaction



(e) $\text{CH}_3\text{CH}_2\text{CHO}$

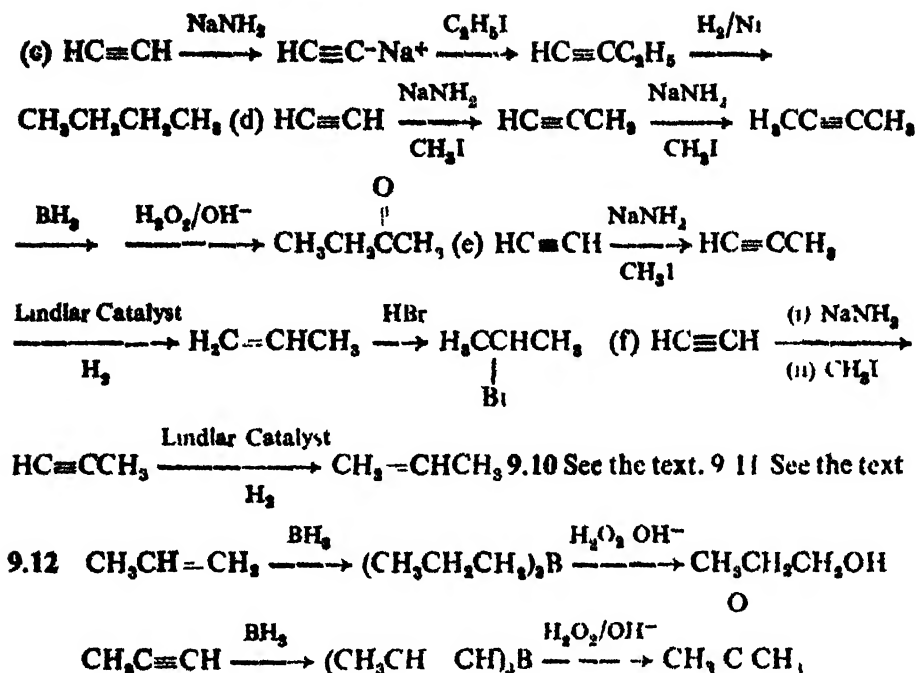


9.3 Acyclic hydrocarbon 9.4 See the text. 9.5 $\text{CH}_3\text{C}\equiv\text{CH}$ 9.6 Propyne forms the red-colored Cu -acetylide, propene a dibromo addition product while propane gives no reaction. 9.7 $\text{H}_3\text{C}-\text{CH}_2-\text{CH}_2-\text{C}\equiv\text{CH}$ 9.8 Three

isomers 9.9 (a) $\text{HC}\equiv\text{CH} \xrightarrow{\text{NaNH}_2} \text{HC}\equiv\text{C}-\text{Na}^+ \xrightarrow{\text{C}_2\text{H}_5\text{I}} \text{HC}\equiv\text{CC}_2\text{H}_5$

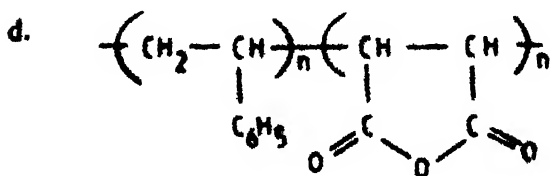
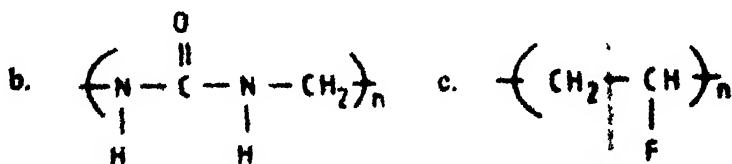
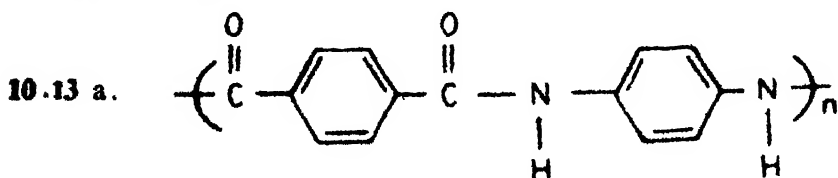
(b) $\text{HC}\equiv\text{CH} \xrightarrow[\text{CH}_3\text{I}]{\text{NaNH}_2} \text{CH}_3\text{C}\equiv\text{CH} \xrightarrow{\text{BH}_3} \begin{array}{c} \text{CH}_3\text{C}-\text{CH} \\ | \quad | \\ \text{H} \quad \text{B} \end{array} \xrightarrow{\text{H}_2\text{O}_2/\text{OH}^-}$

$\text{CH}_3\text{CH}=\text{CH} \xrightarrow{\text{Oxi}} \text{CH}_3\text{CH}_2\text{CHO} \xrightarrow{\text{Oxi}} \text{CH}_3\text{CH}_2\text{COOH}$
 $\quad \quad \quad |$
 $\quad \quad \quad \text{OH}$



CHAPTER 10

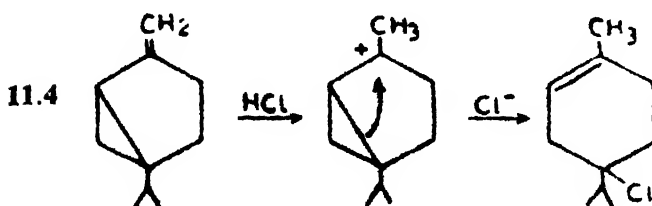
10.1 See the text 10.2 See the text 10.3 See the text 10.4 See the text 10.5 Addition polymer 10.6 To harden and improve its properties 10.7 See the text 10.8 See the text 10.9 Radical initiator, inhibitor, chain transfer, radical initiator 10.10 Coupling, disproportionation and chain transfer reaction 10.11 a. No, b. Yes, makes H-bond with water c. Yes, d. Yes, non-inflammable 10.12 See the text



10.14 Isotactic 10.15 See the text 10.16 See the text

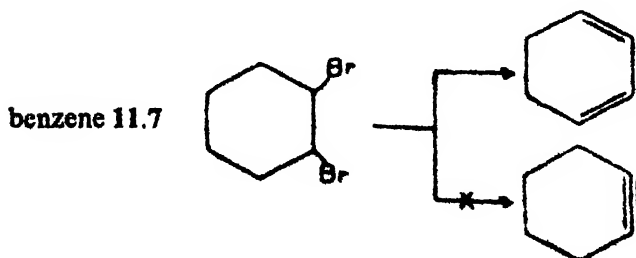
CHAPTER 11

11.1 (a) 2-Methylcyclopentanone (b) *cis*-1,3-Dichlorocyclobutane (c) 3-Oxocarboethoxycyclohexane (d) 4-Chloro-4-methylcyclohexanone (e) *cis*-1-Chloro-4-methylcyclohexane (f) 1-Ethylcycloheptane (g) Cyclopropane carboxyaldehyde (h) Cyclopent-2-en-1-ol (i) Cyclohexylethanamide (j) 2-Cyclobutylethyl chloride (k) 1-Cyclohexenecarboxylic acid (l) 2-Cyclobutyl-3-methyl-1-butene (m) 1,3-Dimethylbicyclo[1.1.0] butane (n) Bicyclo[4.1.0]heptane (o) 7,7-Dimethylbicyclo[2.2.1]hepta-2,5-diene (p) Cyclopentanecarbonitrile (q) *trans*-2-Chloro-1,2-dimethylcyclopentanol 11.2 See the text 11.3 See the text (r) Bicyclo[3.1.0] hexane (s) Bicyclo[4.2.0]octane (7-Methyl bicyclo[2.2.1] hept-2-ene.



11.5 See Sec. 11.3

11.6 (a) Addition of bromine or Bayer's test (b) Same as in (a) (c) Bromination of cyclopropane (d) Same as in a (e) Bromination (Br₂ : Fe) of

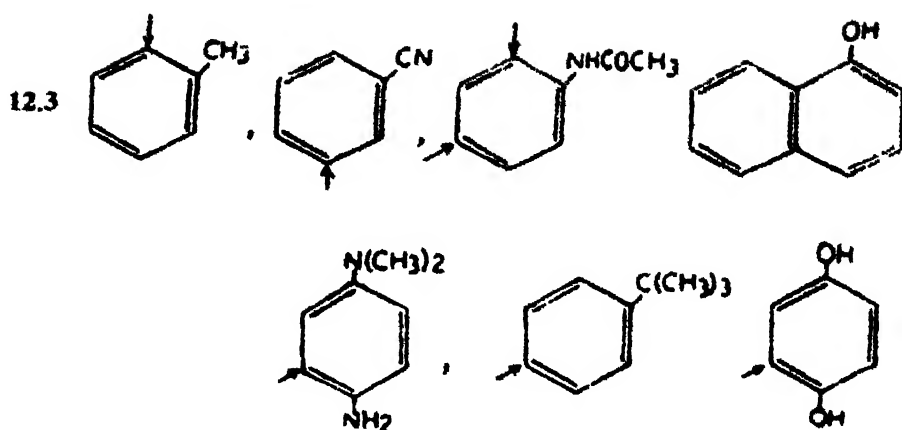


Putting a triple bond in a small ring is energetically unfavorable.

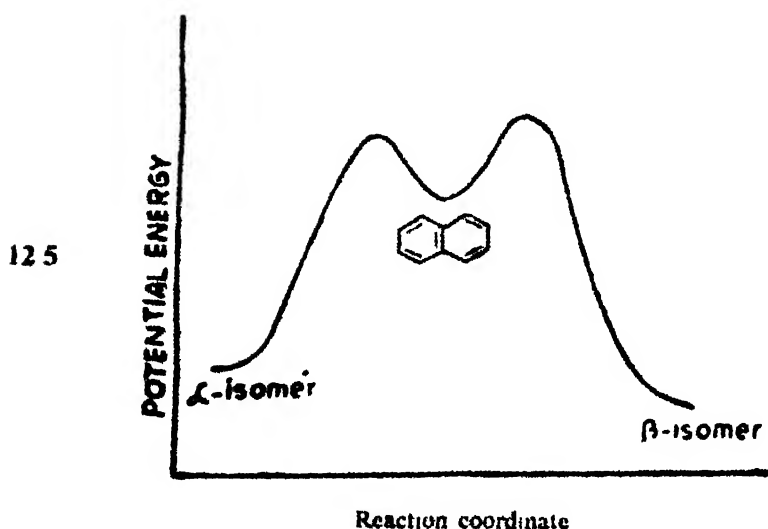
11.8 Because of the presence of large bond angle strain.

CHAPTER 12

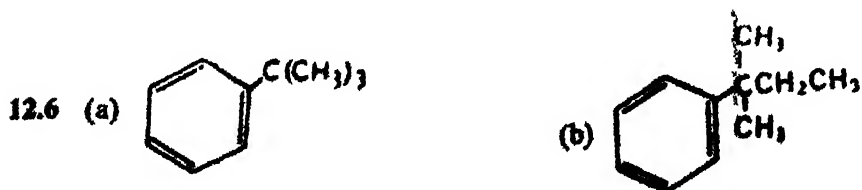
12.1 C₆H₅OH, C₆H₅OCH₃, C₆H₅CH₃, C₆H₆, C₆H₅NO₂ 12.2 Nine isomers

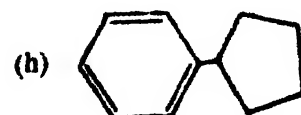
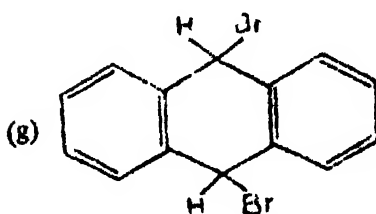
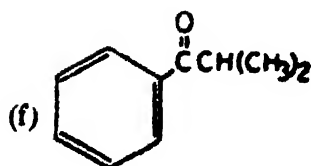
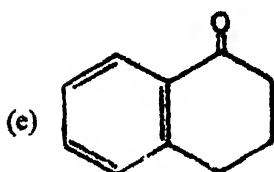
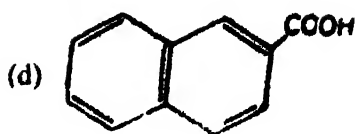
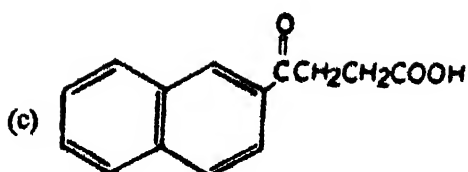


12.4 See Sec. 12.6



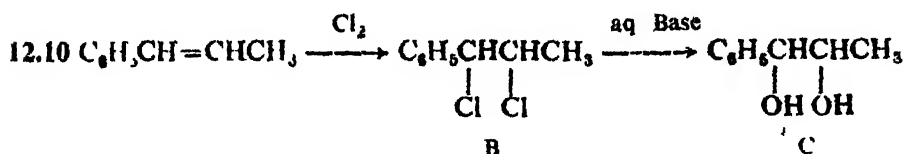
At low temperature α -isomer is formed because the corresponding ion is more stable but the thermodynamically more stable β -isomer results at a high temperature. Its formation requires a higher activation energy compared to the α -isomer



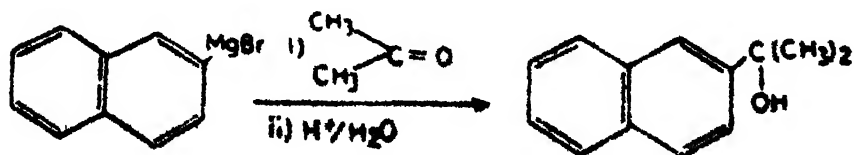


(i) No reaction

12.7 Isomeric xylenes 12.8 See the text 12.9 Slowly, NO_2 deactivating

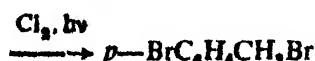
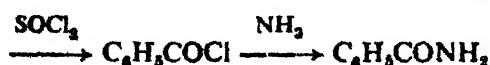
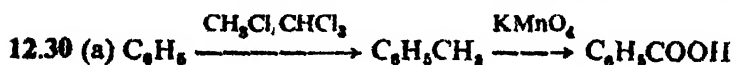


12.11 $\text{o-Xylene} \xrightarrow{\text{Oxi}}$ Phthalic acid 12.12 (a) See the text



12.13 See the text 12.14 See the text 12.15 $-\text{OH}$ is electron-donating group thus activates the ring 12.16 See Sec. 12.5 12.17 See the text 12.18

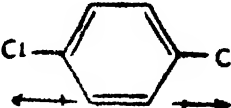
(a) See Sec. 12.9.6 (b) See Sec. 12.9.3 12.19 β -isomer is thermodynamically more stable 12.20 Ethylbenzene and *o*-xylene 12.21 See Sec. 12.5 12.22 See Sec. 12.9.6 12.23 $-\text{NO}_2$ group deactivates the ring 12.24 See the text. 12.25 See the text 12.26 This implies that electrons are delocalized in the ring 12.27 See the text. 12.28 (a) $-\text{CH}_3$ group is an activating (b) $-\text{Cl}$ withdraws electrons inductively (c) *t*-Butyl is an activating group (d) See p. 276 (e) $-\text{NO}_2$ group is a strong deactivating group in the F.C. reaction (f) $-\text{NH}_2$ group complexes with AlCl_3 thus becomes deactivating. 12.29 (a) no (b) no (c) no (d) yes (e) no (f) no (g) no (h) yes (i) yes



CHAPTER 13

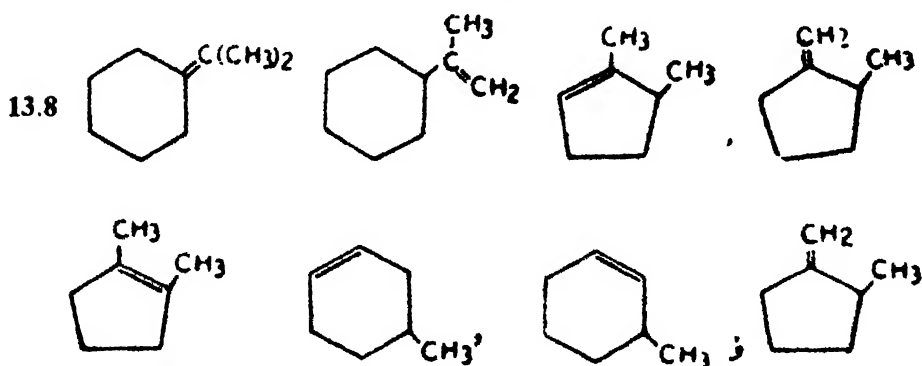
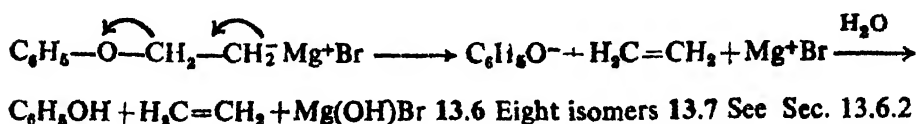


13.2 (i) Kinetics (ii) Stereochemistry (iii) reactant structure (iv) solvent and (v) mechanism 13.3 1-Chloro-2-butene > 1-chlorobutane > 1-chloro-1-butene

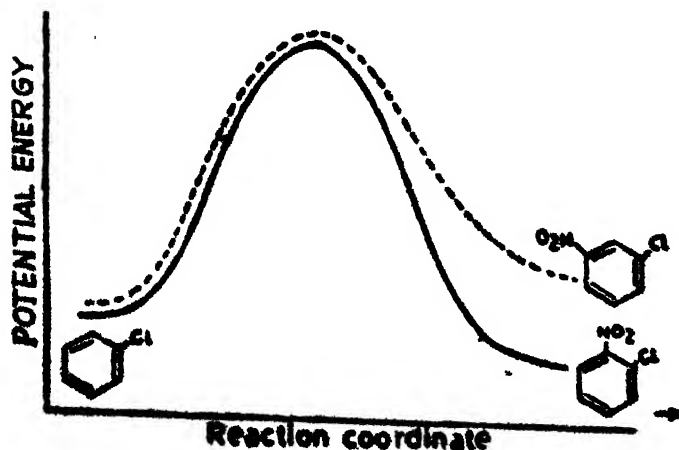
in S_N2 displacement 13.4 (a) In  the two individual

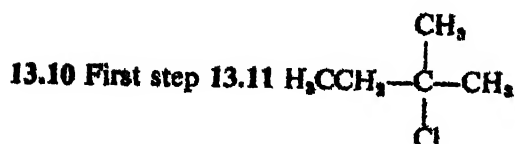
dipoles cancel each other (b) See the text (c) See the text (d) Does not hydrogen-bond with water (e) Because the *m*-nitro group does not activate the ring towards nucleophilic attack. (f) The benzyl cation is stabilized by resonance (g) A better leaving group (h) Steric hindrance to S_N2 attack

(i) It undergoes decomposition. 13.5 $C_6H_5OCH_2CH_2Br \xrightarrow[\text{ether}]{Mg}$



13.9





13.12 wt. of C = 0.00532 g

wt. of H = 0.0089 g

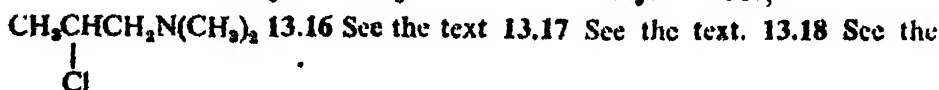
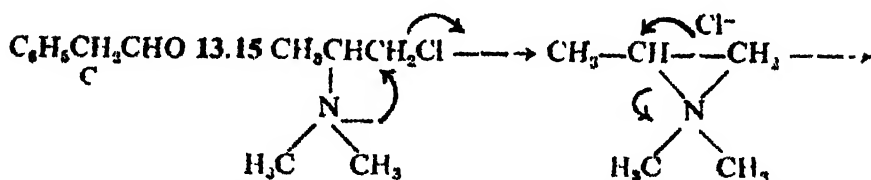
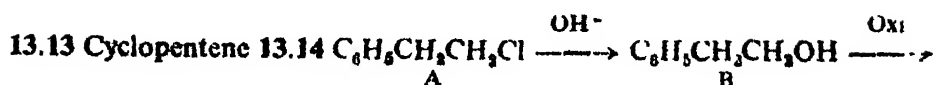
wt. of Cl = 0.22 - (0.0532 + 0.0089) g
= 0.1578 g

E.F. = CH_2Cl

Vol. at NTP = $\frac{37.23 \times 768 \times 273}{760 \times 378} = 27.18 \text{ ml}$

Mol wt. = 98.9

M.F. = $\text{C}_2\text{H}_5\text{Cl}_2$



13.19 See the text 13.20 See Chapter 12. 13.21 See the text. 13.22 Substitution of a methyl group at the C—C bond has a stabilizing effect due to hyperconjugation. 13.23 The CN^- ion can be described by two resonance structures: $\text{:}\ddot{\text{C}}::\text{N:} \longleftrightarrow \text{:C::}\ddot{\text{N}}^-$ in which case a formal negative charge is placed on either C or N atom. 13.24 *m*-Nitro group does not produce the activating effect 13.25 Because the rate depends only on the concentration of *t*-butyl bromide ion ($\text{S}_{\text{N}}1$ reaction). 13.26 Because this is the order of stability of carbocations formed after the cleavage of the C—Cl bond. 13.27 (a) rate = $k [\text{C}_6\text{H}_5\text{CH}_2\text{Cl}] [\text{NaN}_3]$ (b) See the text (c) Doubled.

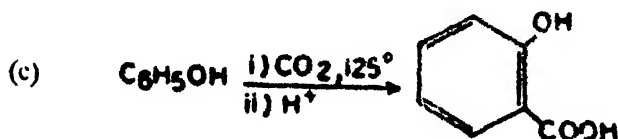
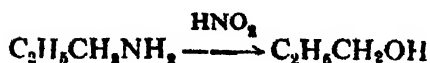
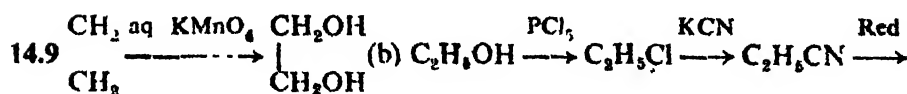
CHAPTER 14

14.1 See the text. 14.2 (a) *o*-Cresol gives coloration with FeCl_3 (b) Phenol gives coloration with FeCl_3 (c) Ethyl acetate responds to iodoform test (d) 1-Pentanol responds to iodoform test (e) Phenol gives coloration with FeCl_3

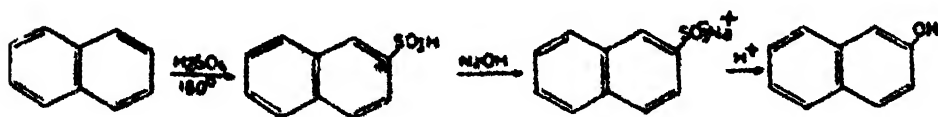
14.3 Eight isomers 14.4 $(\text{CH}_3)_3\text{CBr}$, $(\text{CH}_3)_2\text{C}=\text{CH}_2$; $(\text{CH}_3)_3\text{COCOCH}_3$, $(\text{CH}_3)_3\text{CO}^-\text{Na}^+$, CH_4 , no reaction. 14.5 See the text 14.6 $(\text{C}_6\text{H}_5)_2\text{CCH}_2\text{OH}$, $< (\text{C}_6\text{H}_5)\text{CHOHCH}_3 < (\text{C}_6\text{H}_5)_2\text{COHCH}_3$. 14.7 (a) It loses the aromatic stabilization (b) The alkene is more stable due to resonance (c) Because the other products are gaseous (d) 2-Methyl-2-pentanol yields a stable olefin (e) The phenoxide ion is stabilized by resonance (f) Ethanol contains

the $\text{H}-\underset{\text{CH}_3}{\overset{|}{\text{C}}}-\text{OH}$ grouping (g) Forms a stable tertiary carbonium ion.

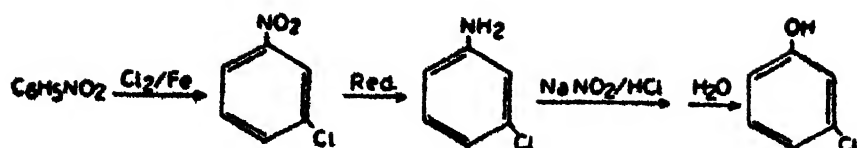
14.8	$\text{C}_2\text{H}_5\text{OH}$	$\text{C}_6\text{H}_5\text{OH}$
K	H_2 evolved	no reaction
NaOH	no reaction	forms salt
PBr_3	forms bromide	no reaction
HBr	forms bromide	no reaction
PCl_5	forms chloride	no reaction
SOCl_2	forms chloride	no reaction
$\text{CH}_3\text{COOH}/\text{H}^+$	forms acetate	forms acetate



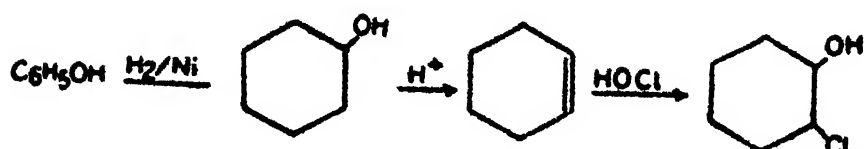
(d)



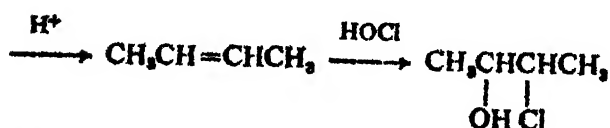
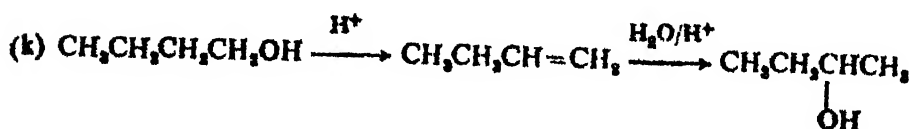
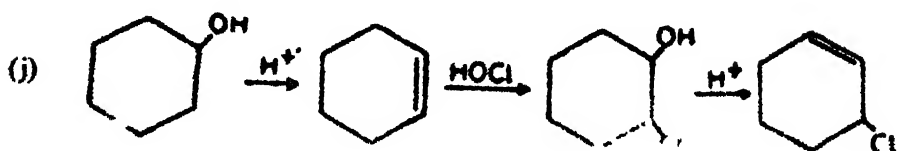
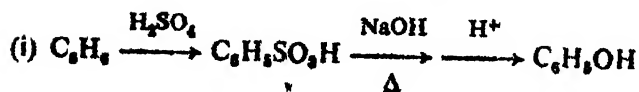
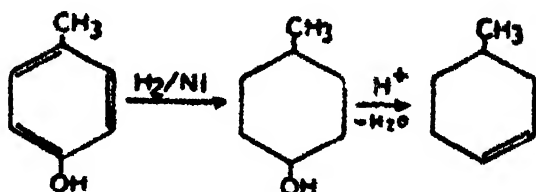
(f)



(g)



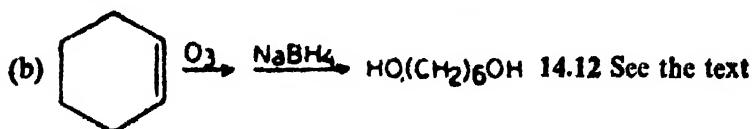
(h)



14.10



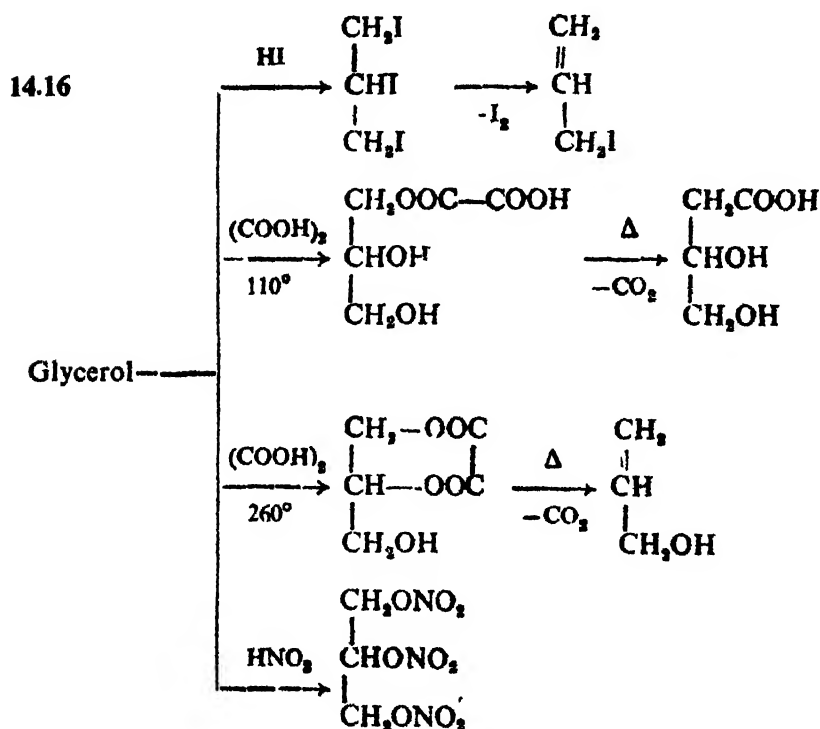
14.11 (a) Because of intramolecular hydrogen-bonding



14.13

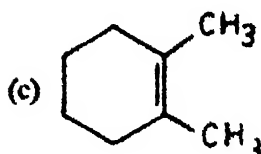
	C_6H_5OH	C_2H_5OH
$FeCl_3$	Coloration	No color
Oxidation	No reaction	Oxidized to aldehyde
Na	No reaction	Evolves H_2 gas
Br_2	A solid derivative	No reaction
HBr	No reaction	A bromide

14.14 See the text 14.15 See Sec. 14.11.



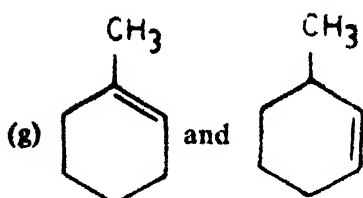
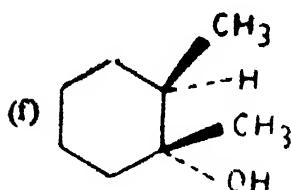
14.17 See the text 14.18 See the text 14.19 See the text

14.20 (a) No reaction (b) Benzoic acid

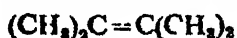


(d) 1,3,5-Trimethylbenzene

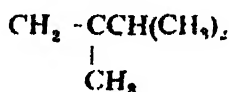
(e) Cyclohexyl chloride



14.21 Hydration, hydroboration and oxymercuration of alkenes 14.22. The initially formed carbocation undergoes a $-\text{CH}_3$ shift to form



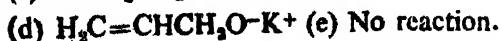
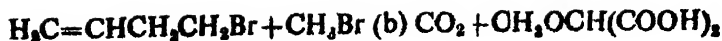
and



14.23 $(\text{CH}_3)_3\text{COH}$.

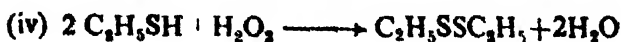
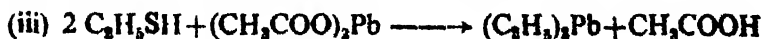
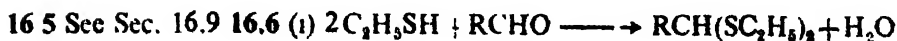
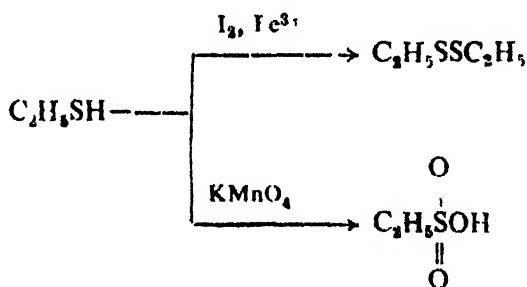
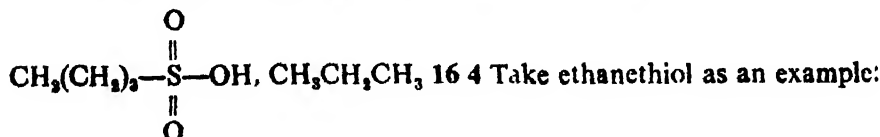
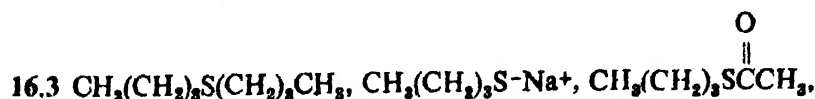
CHAPTER 15

15.1 (a) Propylene oxide (b) *m*-chloroanisole (c) *bis*- β -Methoxyethyl ether (diglyme) (d) Dimethylene-di-bromo ether (e) Cyclohexyl *t*-butyl ether (f) Ethoxycyclohexane (g) *iso*-Propyl ether (h) *p*-Bromophenetole (i) 1-Ethoxy-2-methoxycyclobutane (j) 1-*iso*-Propoxymethylenecyclohexanone. 15.2 In THF, in contrast to furan the electron pairs are available for H-bonding with water 15.3 (a) Ethanol gives iodoform test (b) Ethoxyethanol gives the iodoform test (c) Butyl iodide with AgNO_3 yields AgI. (d) Ethyl allyl ether decolorizes bromine water (e) *p*-Methoxyphenol gives coloration with FeCl_3 . 15.4 See the text 15.5 See Sec. 15.8 15.6 Four isomers 15.7 $\text{HOCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OH}$ 15.8 $\text{CH}_3\text{CH}_2\text{OCH}_3$ (a) 15.9



CHAPTER 16

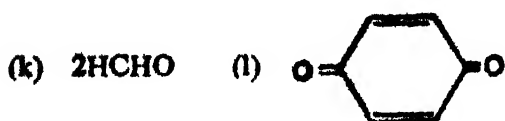
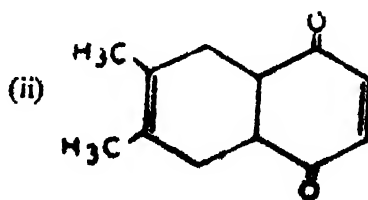
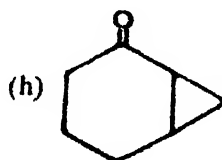
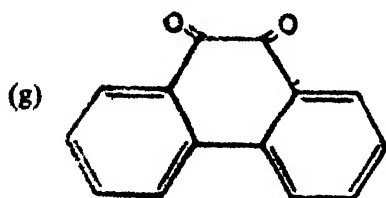
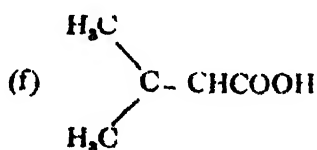
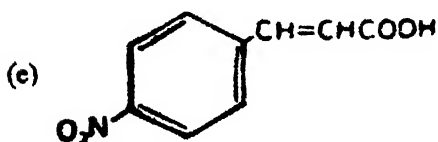
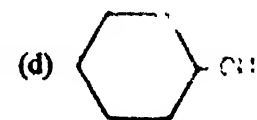
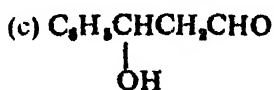
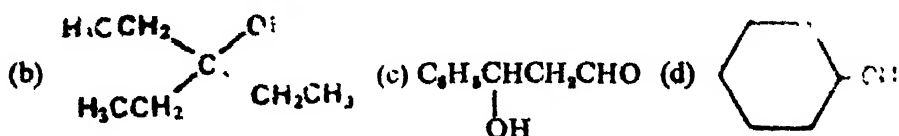
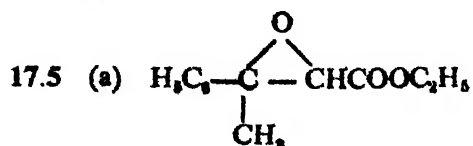
16.1 (a) 2-Methoxy-3,3,N,N-tetramethyl-1-butanamine (b) 4-Nitrobutanethiol (c) 1-(Ethylthio) propane (d) 2-Butanethiol (e) *o*-Ethylbenzenethiol (f) 3-Ethoxy-N,N,2-trimethylpropanamide (g) 2-Methyl-1-(methylthio)-butane (h) 1-Dodecanethiol 16.2 See the text

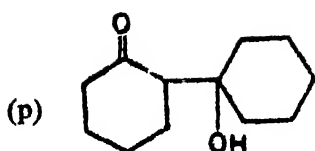


CHAPTER 17

17.1 (a) Methyl ethyl ketone (b) 4-Methyl pentanal (c) 2-Chlorocyclopentanone (d) 3-Methylcyclohexanecarboxaldehyde (e) *p*-Nitrobenzaldehyde (f) *m*-Bromoacetophenone (g) Propenal (h) Salicylaldehyde (i) Ethyl 3-formylpropanoate (j) 6-Oxo-octanal (k) 1,1-Dimethoxyethane 17.2 See the text

17.3 (a) Benzaldehyde does not possess an α -carbon atom (b) It forms intra-molecular H-bonding (c) 1-Butanol is more polar (d) It contains an active methylene group (e) Because the protonated ketone is highly stabilized by resonance (f) Clemmensen reduction is subject to steric hindrance (g) Because hydroxylamine is stable as its hydrochloride (h) Electron-donating effect of $-\text{OCH}_3$ group reduces the electrophilicity of the carbonyl carbon atom (i) Because of steric hindrance. 17.4 Because an α -hydrogen atom is acidic



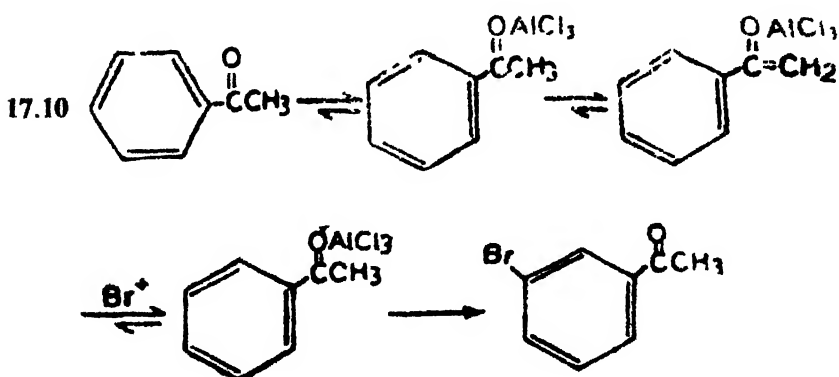


(q) $p\text{-ClC}_6\text{H}_4\text{CHO}$ (r) alkylation

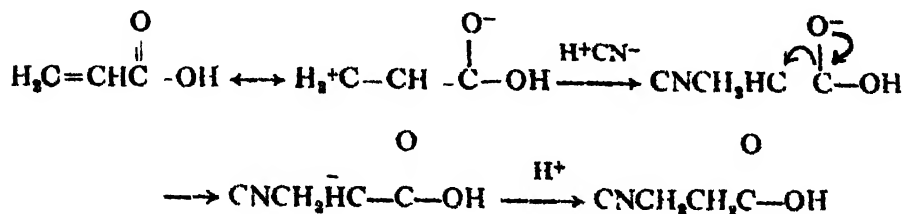
(s) $(\text{CH}_3)_3\text{C}-\overset{\text{O}}{\parallel}\text{C}-\text{C}_6\text{H}_5$ (t) $(\text{CH}_3)_3\text{CCOOH} + (\text{CH}_3)_3\text{CCH}_2\text{OH}$

17.6 2-Butanol, Acetone, 2-Pentanone 1-Phenylethanol 17.7 See the text

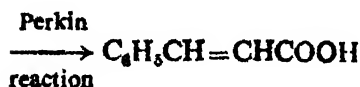
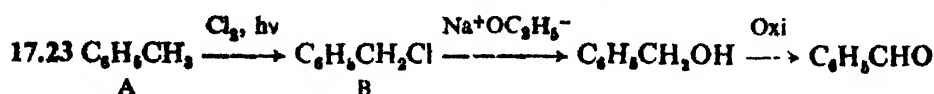
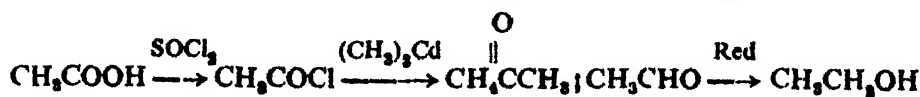
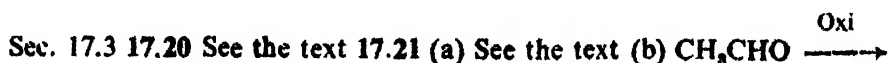
17 8 See the text 17.9 C_6H_5CHO



In large quantities, AlCl_3 complexes with $\text{C}=\text{O}$ group to give *m*-bromoacetophenone. In small amounts, however, it acts as a catalyst to form phenacylbromide 17.11 di-*t*-Butyl ketone, methyl *t*-butyl ketone, acetone, acetaldehyde 17.12 (a) Propanal gives Tollens' test (b) Acetone forms iodoform (c) Acetaldehyde responds to iodoform test (d) 4-Pentyn-2-one forms an acetylide (e) Acetone forms iodoform (f) 4-Bromo-2-butanone forms iodoform (g) 2-Pentanone yields iodoform 17.13 In the case of the acid the double bond is activated due to the presence of a $-\text{COOH}$ group.

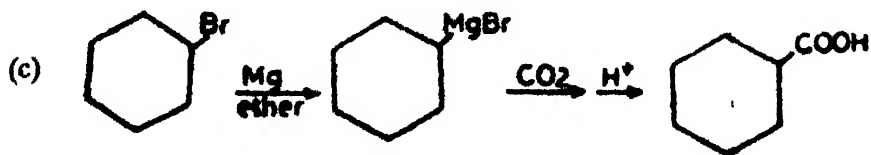
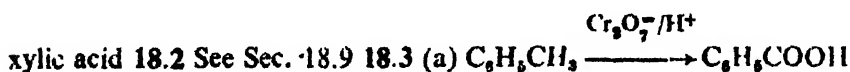


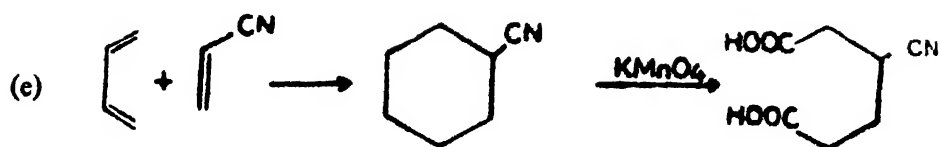
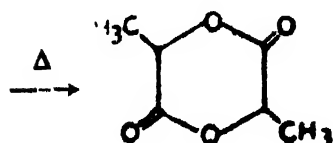
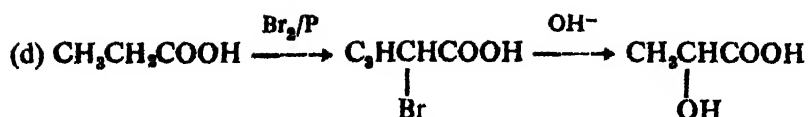
17.14 (a) See the text, (b) $\text{C}_6\text{H}_6 \xrightarrow{\text{CH}_3\text{Cl}, \text{AlCl}_3} \text{C}_6\text{H}_5\text{CH}_3 \xrightarrow{\text{KMnO}_4/\text{OH}^-} \text{C}_6\text{H}_5\text{COOH}$



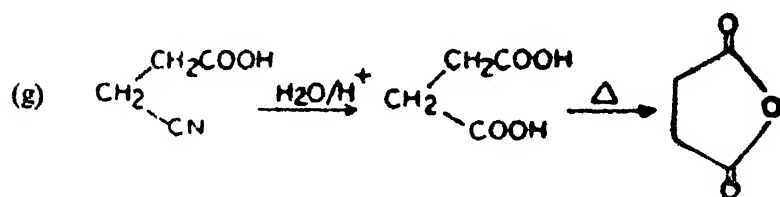
CHAPTER 18

18.1 (a) 2-Butenoic acid (b) 2-Cyclohexenecarboxylic acid (c) 2-Cyclopropylpropanoic acid (d) Benzoic anhydride (e) 2,2-Dichloroethanoic acid (f) 1,5-pentanedioic acid (g) N-ethylethanamide (h) 5-Oxo-pent-2-enoic acid (i) *p*-Toluic acid (j) Cyclohexyl benzoate (k) *trans*-2-Methylcyclohexanecarboxylic acid

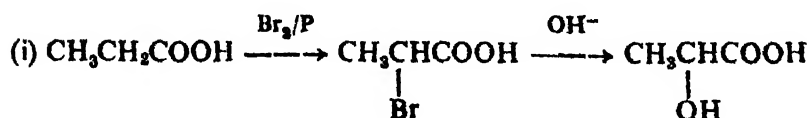
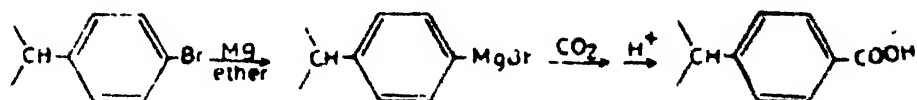


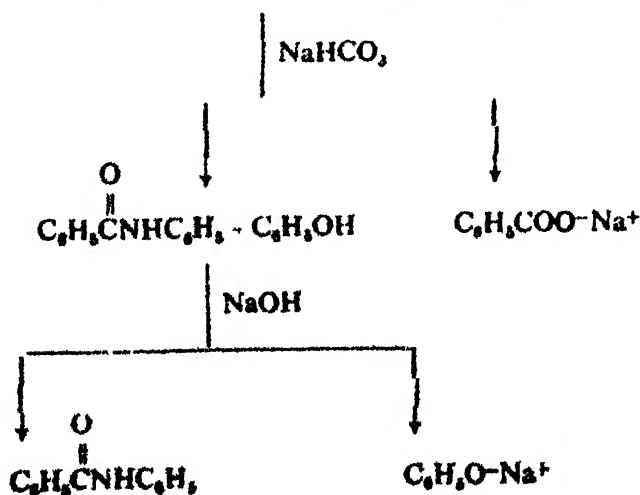
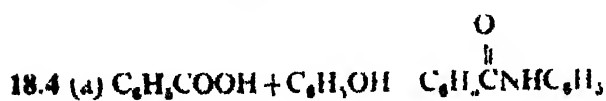
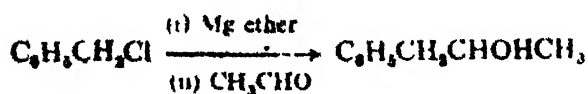
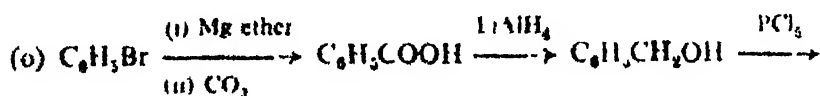
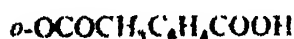
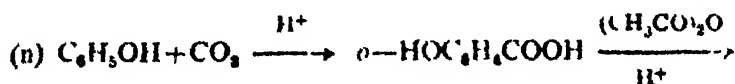
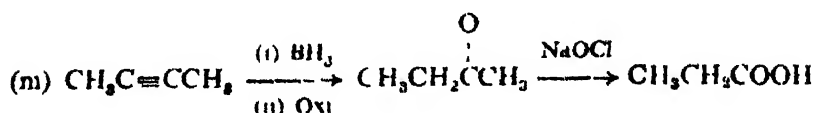
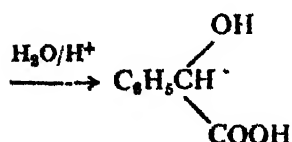
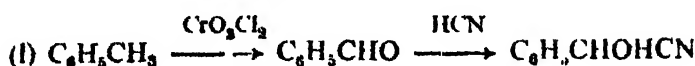
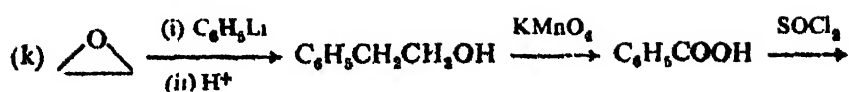


(f)

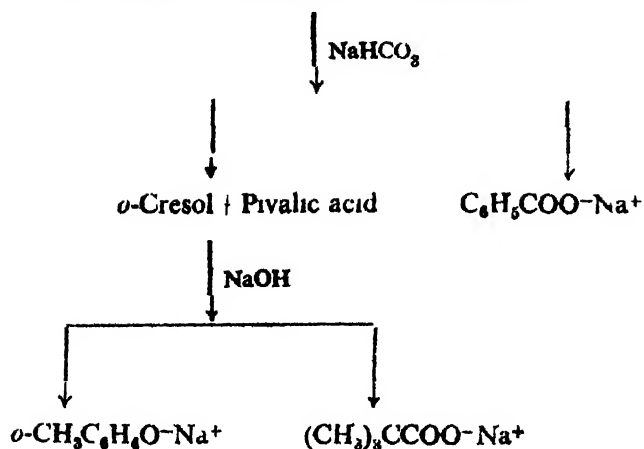


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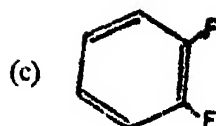
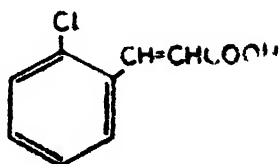




(b) *o*-Cresol + Benzoic acid + Pivalic acid

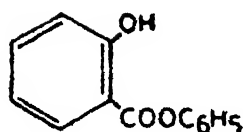


18.5 (a) $\text{HO}(\text{CH}_2)_6\text{COOH}$



(d) $\text{C}_6\text{H}_5\text{CH}(\text{Br})\text{COOH}$

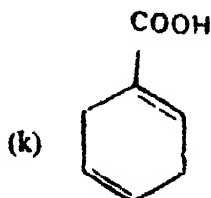
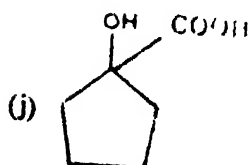
(e) $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$



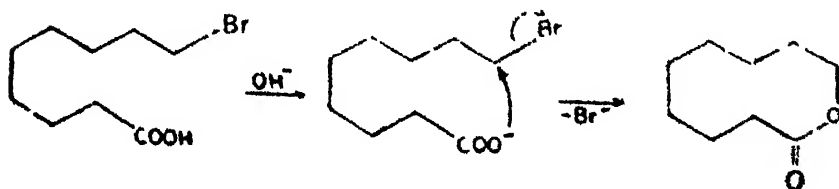
(g) $\text{C}_6\text{H}_5\text{CH}(\text{OH})\text{CH}(\text{CH}_3)\text{COOC}_2\text{H}_5$

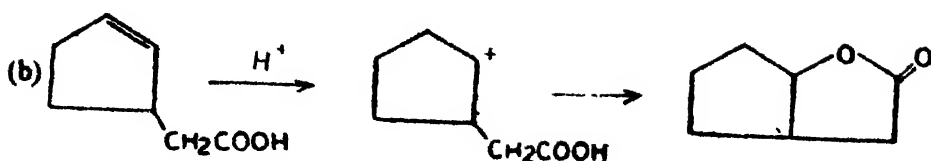


(i) $\text{CO}_2 + \text{H}_2\text{O}$

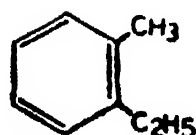


18.6 (a)





18.7 See Sec. 18.5 18.8 $\text{CH}_3\text{CH}_2\text{CH}_2\overset{\text{O}}{\parallel}\text{CCH}_3$ 18.9



18.10 (a) Formic acid decolorizes aqueous KMnO_4 solution (b) Lactic acid responds to iodoform test (c) Crotonic acid decolorizes KMnO_4 solution (d) Acetyl chloride evolves heat on adding water 18.11 Molecular formula $\text{C}_7\text{H}_6\text{O}_4$

3.312 mg of the acid $7.34 \times .01$ mg of NaOH

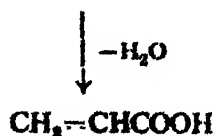
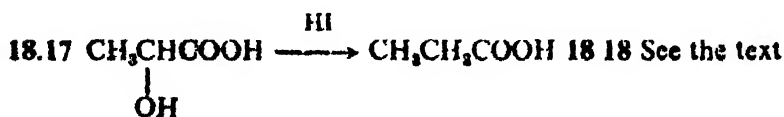
105 " " $7.33 \times .01$ mg of COOH

$$\frac{7.33 \times .01 \times 45 \times 10^4}{3.312}$$

Now 45 g one COOH group

\times 2 COOH groups

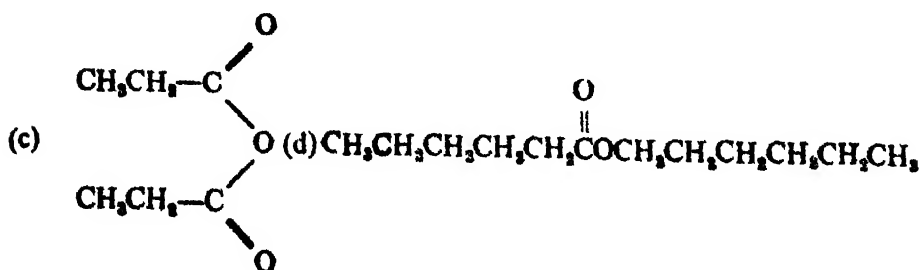
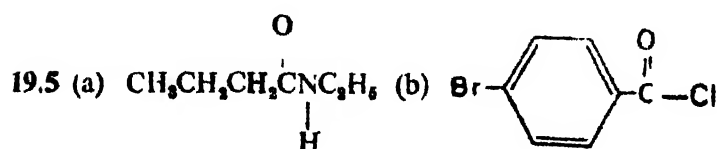
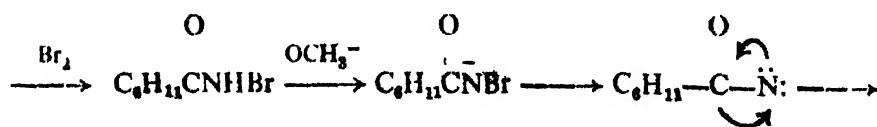
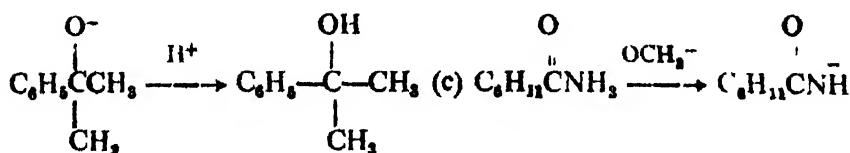
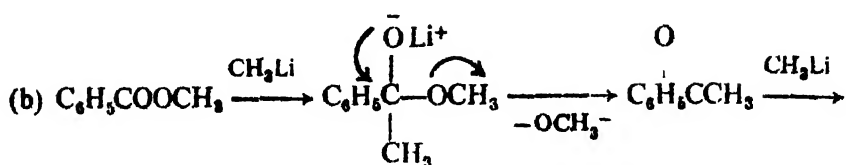
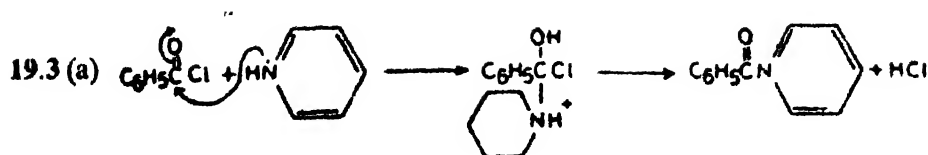
18.12 See Sec. 18.15.2 18.13 See Sec. 18.15.1 18.14 (a) See the text (b) See the text 18.15 See Sec. 18.5 18.16 See Sec. 18.8

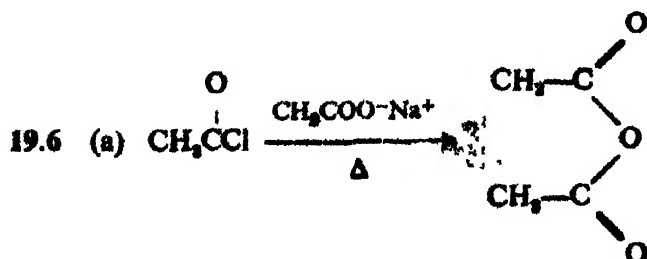
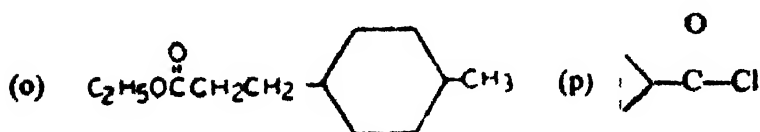
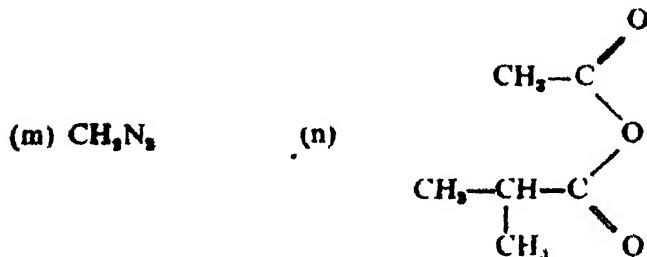
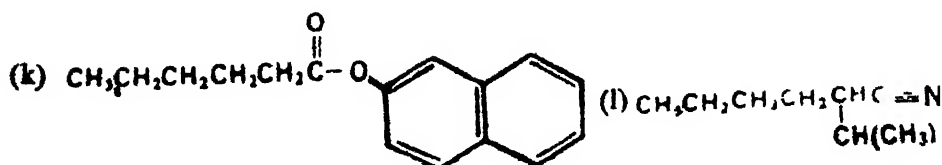
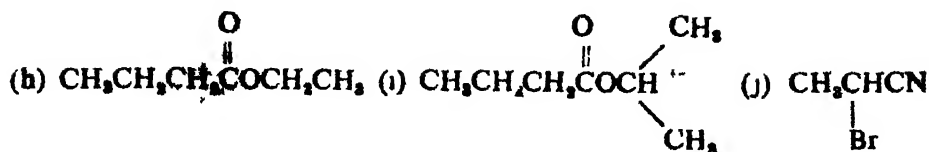
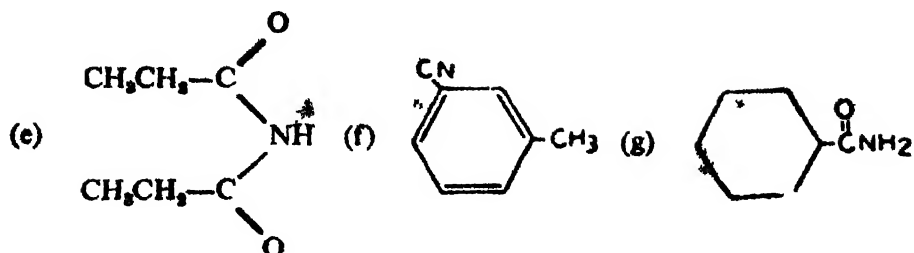


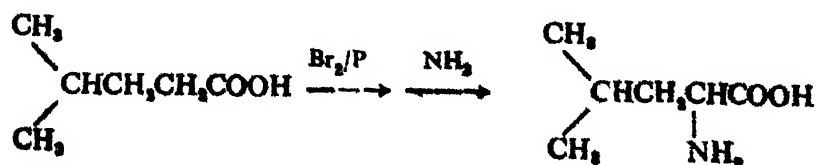
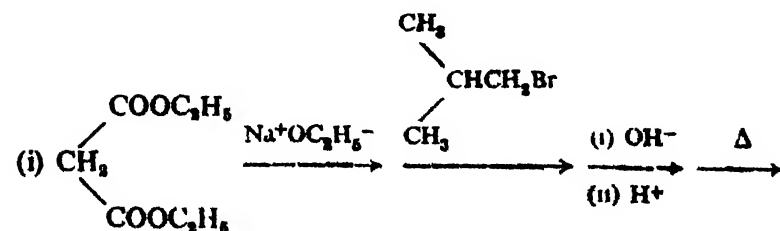
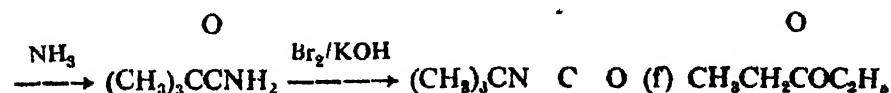
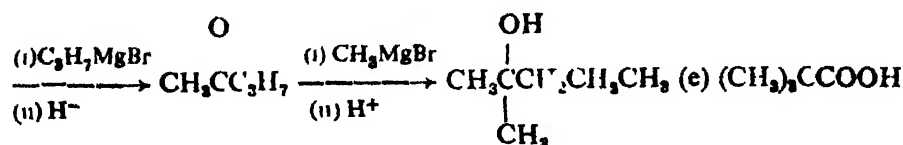
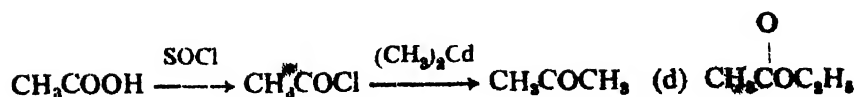
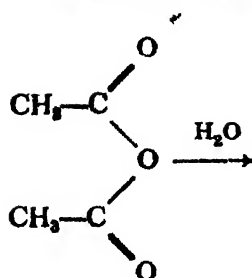
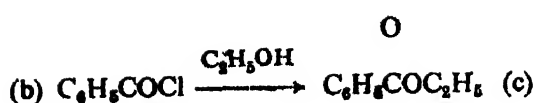
18.19 See Sec. 18.15.3 18.20 See the text 18.21 See the text

CHAPTER 19

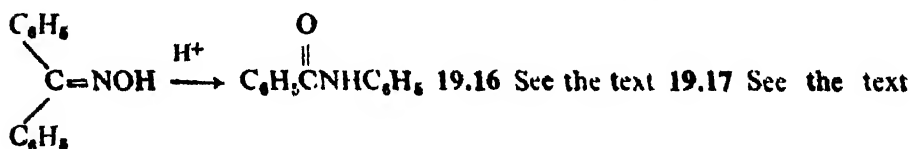
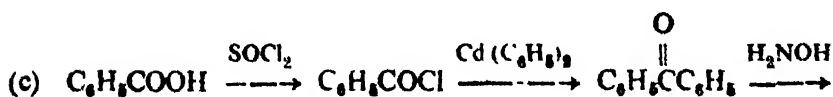
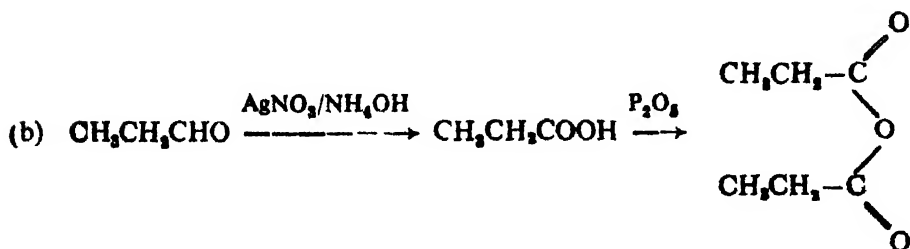
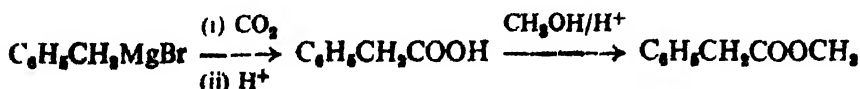
19.1 See the text 19.2 See Sec. 18.10







$\text{CH}_3\text{COC}_2\text{H}_5$ (delocalization of charge) 19.14 $\text{H}_2\text{C}=\text{CHCH}_2\text{CN}$ (base),
 $\text{BrCH}_2\text{CH}_2\text{CN}$ (acid), $\text{CH}_3\text{CH}=\text{CHCH}_2\text{CH}_2\text{CN}$ (base)



19.18 See the text 19.19 See the text 19.20 See the text 19.21 See the text
 19.22 See the text 19.23 See the text 19.24 See the text.

19.25 Mol. weight of tristearin = 890

$$\text{Saponification No.} = \frac{168}{800} \times 1000 = 188.7$$

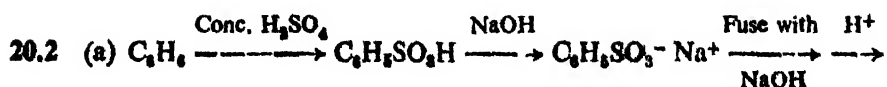
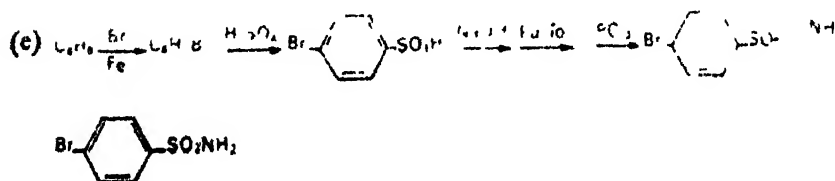
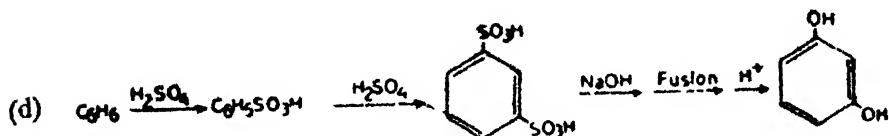
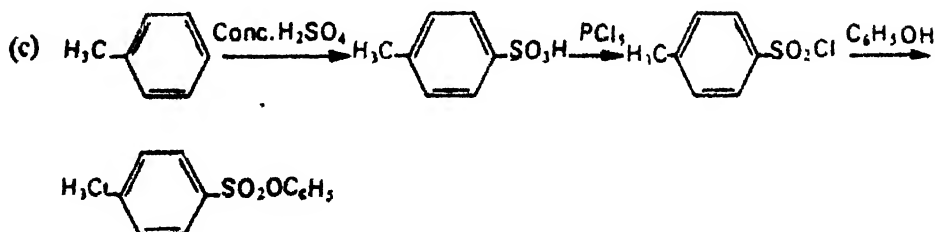
$$\text{Saponification No. of 90\% purity} = \frac{188.7}{100} \times 90 = 170$$

19.26 See the text.

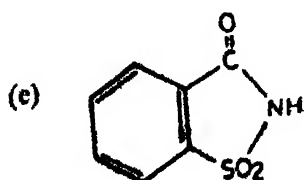
CHAPTER 20

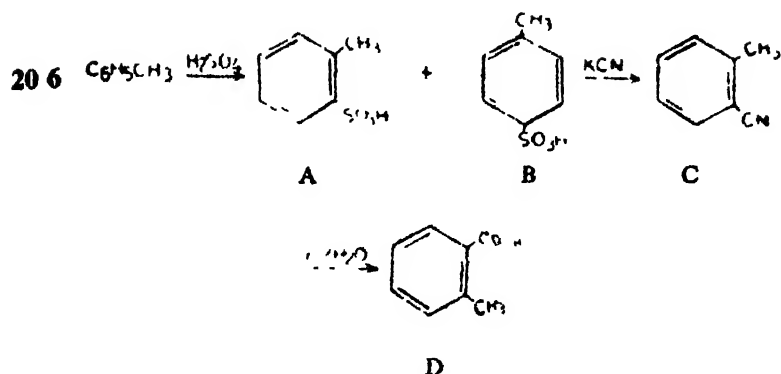
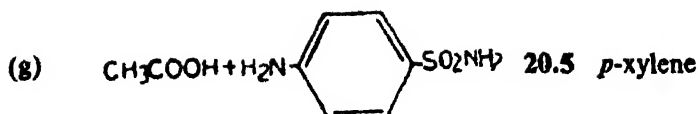
20.1 (a) No reaction (b) $\text{C}_6\text{H}_5\text{SO}_3^- \text{Na}^+$ (c) $\text{C}_6\text{H}_5\text{SO}_3^- \text{Na}^+$

(d) $m\text{-BrC}_6\text{H}_4\text{SO}_3\text{H}$ (e) CO_2 , $\text{C}_6\text{H}_5\text{SO}_3^- \text{Na}^+$ (f) C_6H_5 (desulfonation)

(g) no reaction (h) $m\text{-C}_6\text{H}_4(\text{SO}_3\text{H})_2$ (i) $\text{C}_6\text{H}_5\text{SO}_3^-$ and H_3O^+ (j) $(\text{C}_6\text{H}_5\text{SO}_3)_2\text{-Ca}^{++}$  $\text{C}_6\text{H}_5\text{OH}$ (b) $\text{C}_6\text{H}_5\text{CH}_3$ same as in (a)

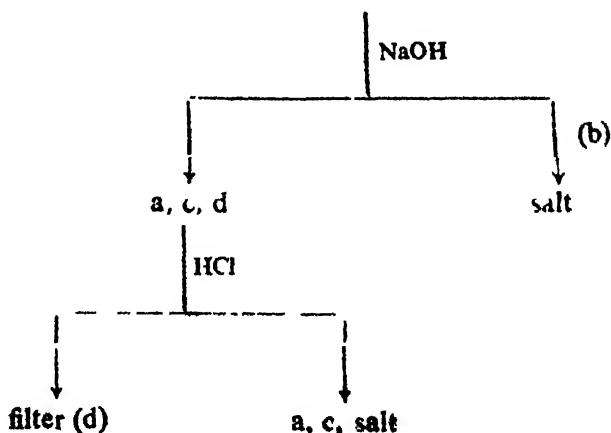
20.3 (a) *o, p* (b) *p* (c) *o, p* (d) *o* (e) *o* (f) *m* (g) *o* 20.4 (a) *m*-Xylene
 (b) $\text{C}_6\text{H}_5\text{SO}_3\text{O}^- \text{Na}^+$ (c) no reaction (d) *m*-Nitrobenzenesulfonic acid

(f) *o*-Tolylsulfonic acid



20.7 Aniline + *p*-Methylbenzenesulfonamide + Sulfanilamide + N, N-Dimethylbenzenesulfonamide

(a) (b) (c) (d)

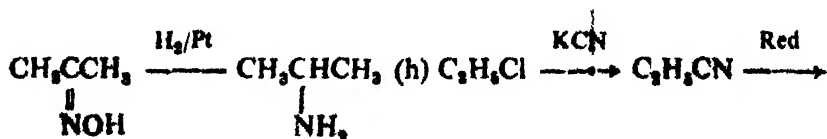
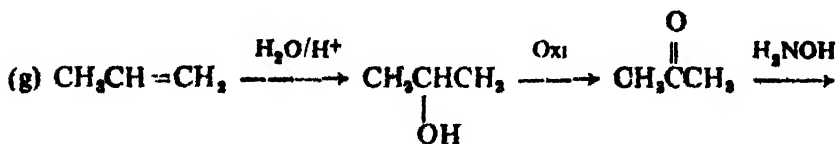
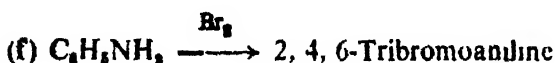
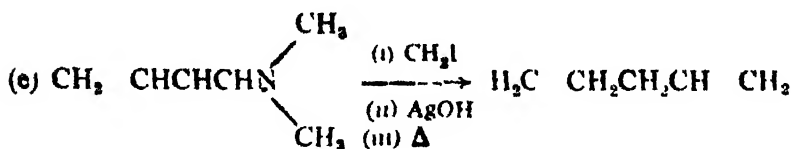
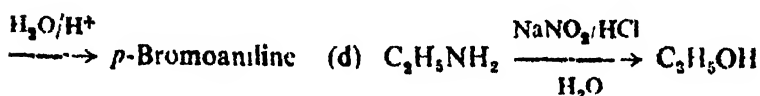
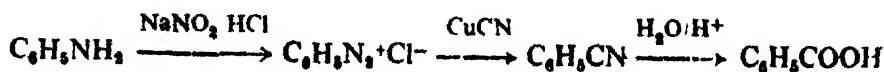
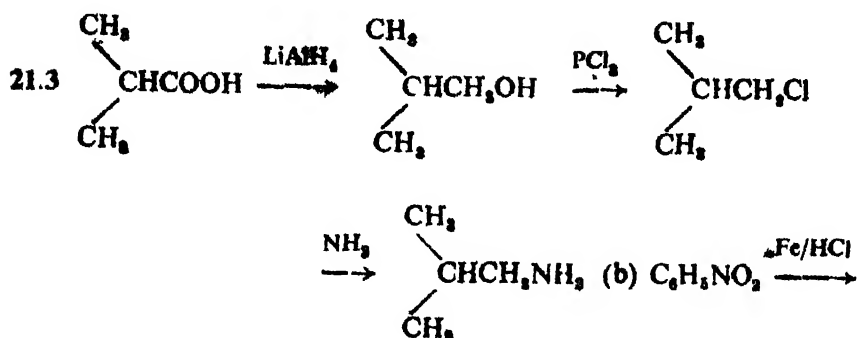


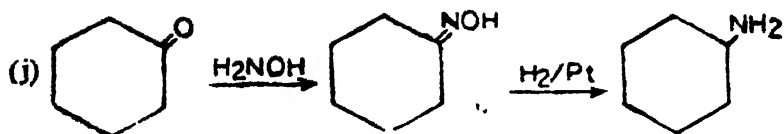
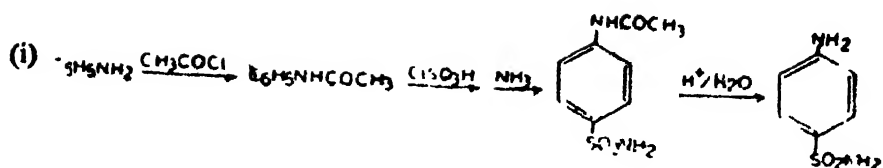
20.8 See the text 20.9 See the text 20.10 See the text 20.11 See the text 20.12 See the text.

CHAPTER 21

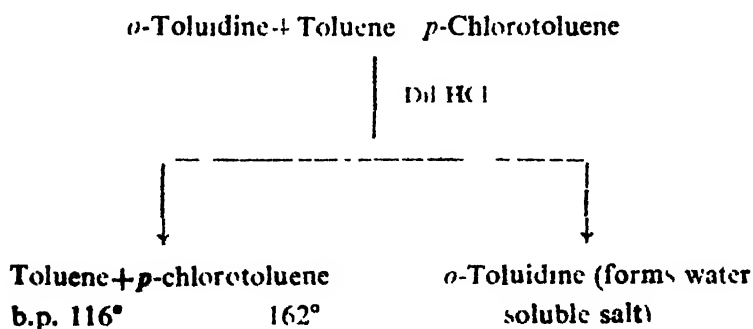
21.1 (a) N, N-dimethylcyclohexylamine (b) *o*-Chloroaniline (c) N, N-dimethylamino-3-methoxypropane (d) 1-Amino-5,5-dichloro-2-pentene (e) Ethanolamine (f) N-cyclohexyl ethanamide (g) N-methylpyrrolidine (h) *m*-Toluidine (i) Tetramethylammonium chloride

- (j) 4-Aminocyclohexaneacetic acid (k) N,N-dimethylaminoethene
 (l) 3-Dimethylamino-1-propanol 21.2 See the text

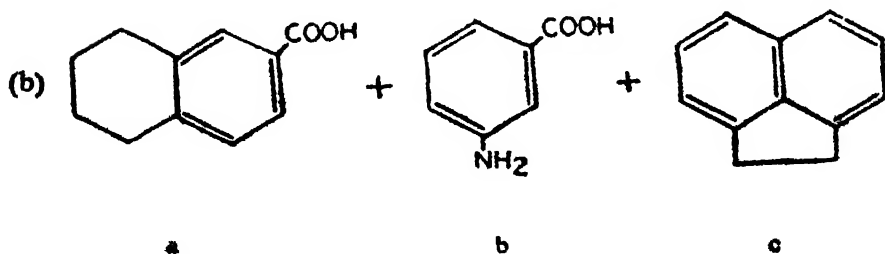


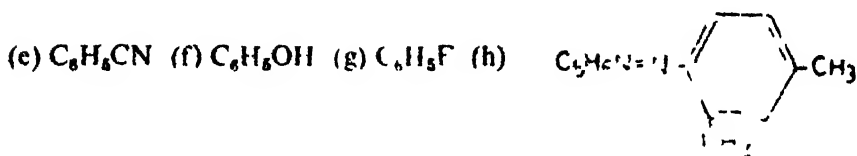
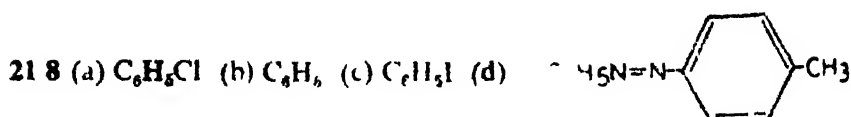
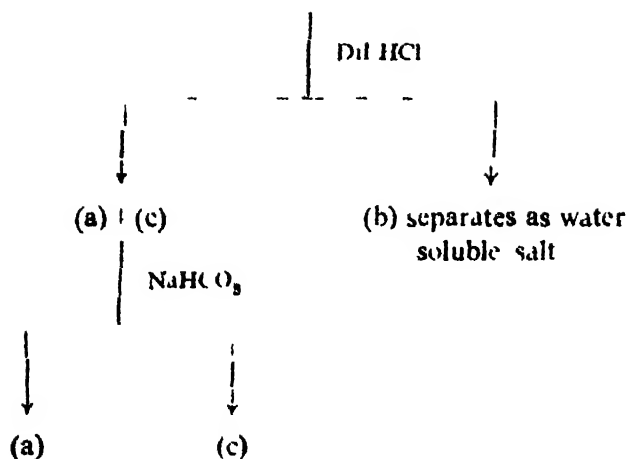


- 21.4 (a) $\text{C}_6\text{H}_5\text{SO}_3^-\text{Na}^+\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ (b) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{NHCOCH}_3$
 (c) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2$ (d) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$
 (e) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2 + \text{HSO}_4^-$ (f) no reaction (g) no reaction
 (h) $\text{HOCH}_2\text{CH}_2\text{NHCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ 21.5 ClNH_2 is a weaker base, because Cl is electron-withdrawing 21.6 Five isomers 21.7 (a)



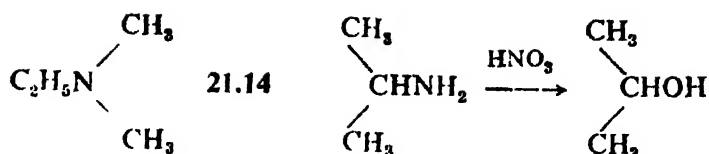
Fractionally distilled





(i) C_6H_5Br 21 9 (a) Because the molecule can flip and the two forms are superimposable (b) Nitrogen is less electronegative than oxygen, thus methylamine has a larger tendency to donate electrons (c) Because of steric hindrance to protonation in $(CH_3)_3N$ (d) Does not possess a hydrogen atom to form the sod. salt (e) The amide group is only moderately activating compared to $-NH_2$ (f) Does not have a hydrogen atom (g) It can undergo oxidation to *p*-quinone 21 10 (a) Cyclopentene (b) 1, 4-Pentadiene (c) Cyclopentene 2, 4-Pentadiene + 1, 3-Pentadiene (d) *iso*-Butylene

21.11 (a) Ethylamine (b) *iso*-Butylamine (c) Dimethylamine (d) *iso*-Propylmethylamine
21.12 (a) Aniline decolorizes bromine water (b) Sulfonamide of propylamine is soluble in water (c) Aniline hydrochloride gives white ppt. with AgNO_3 (e) Hinsberg test (f) *o*-Toluidine is soluble in dil HCl (g) Phenol gives color with FeCl_3
21.13 Since it does not undergo reaction with nitrous acid it is a tertiary amine


21.15 *Amides*
Amines

- | | |
|--|--|
| (i) Insoluble in aq mineral acids | Soluble |
| (ii) Slightly acidic | Basic |
| (iii) Hydrolyzed by an acid or base | Not hydrolyzed |
| (iv) Not oxidized | Oxidized by nitric acid to amine oxide |
| (v) Not acetylated | Acetylated with acetic anhydride |
| (vi) Reduced by LiAlH_4 to amines | No reaction |

21.16 Volume of 0.05 M acid consumed by ammonia – 25 ml

$$\% \text{ of N}_2 = \frac{28 \times 0.05 \times 25 \times 100}{0.303 \times 1000} = 11.6$$

$$\% \text{ of O}_2 = 100 - (69.4 + 5.8 + 11.6) = 13.2$$

Gram atomic ratio:

$$\text{C} : \text{H} : \text{O} : \text{N} = \frac{69.4}{12} : \frac{5.8}{1} : \frac{13.2}{16} : \frac{11.6}{14} = 7 : 7 : 1 : 1$$

Empirical formula $\text{C}_7\text{H}_7\text{ON}$

Molecular weight = 121

Empirical formula weight = 121

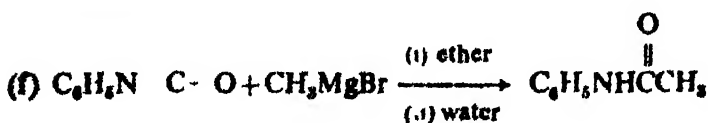
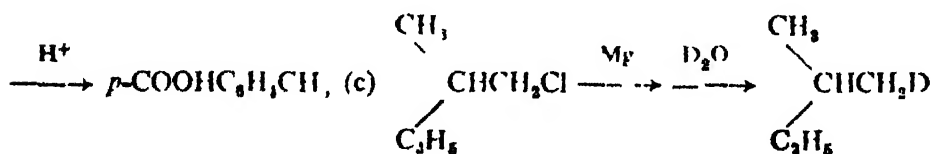
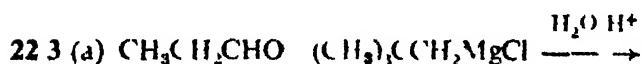
Molecular formula $\text{C}_7\text{H}_7\text{ON}$

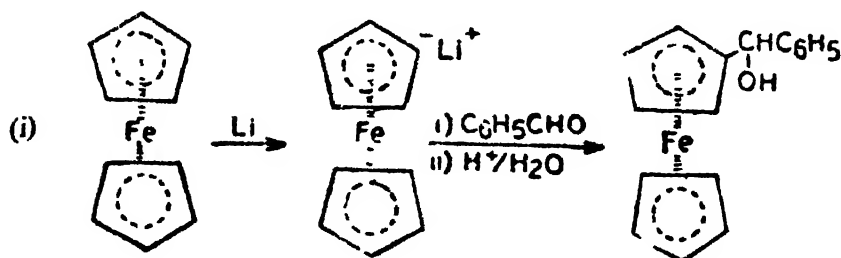
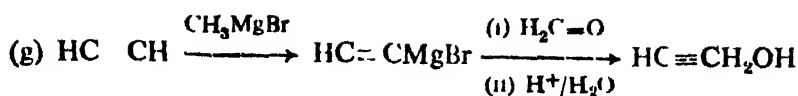
21.17 See Sec. 21.14.1 **21.18** See the text **21.19** See Sec. 21.12 **21.20** See the text **21.21** See the text **21.22** See the text **21.23** See the text **21.24** See the

text **21.25** See the text **21.26** $(\text{CH}_3)_3\text{CCl} \xrightarrow{\text{AgNO}_3} (\text{CH}_3)_3\text{CNO}_2$

$\xrightarrow{\text{Red}} (\text{CH}_3)_3\text{CNH}_2 \xrightarrow{\text{HNO}_3} (\text{CH}_3)_3\text{COH}$ **21.27** See the text **21.28** See the text **21.29** See Sec. 21.12 **21.30** See the text **21.31** (a) Diazonium salt (b) N-methyl-N-nitrosoamine (c) *p*-Nitroso-N, N-dimethylaniline **21.32** (a) Butylamine (b) Pentamethylenediamine (c) *o*-Toluidine (d) Ethylamine **21.33** N, N-dimethylaniline because coupling of benzene diazonium

22 1 (a) CH_4 (b) $(\text{CH}_3)_3\text{COH}$ (c) $\text{CH}_3\text{CH}_2\overset{\text{O}}{\underset{|}{\text{C}}}\text{CH}_3$ (d) $\text{CH}_3\text{CH}_2\text{OH}$

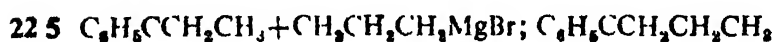




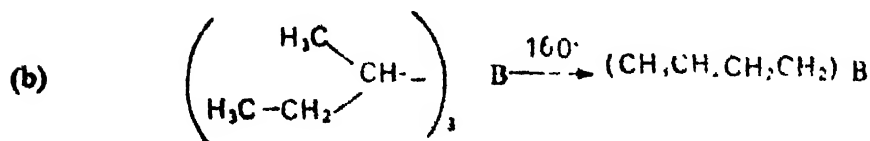
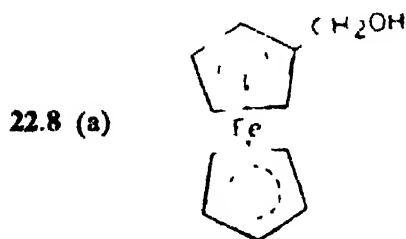
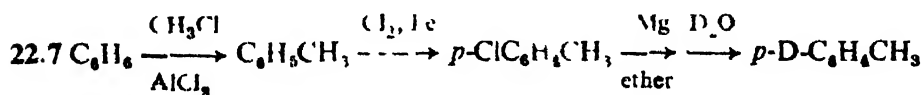
22.4 It undergoes electrophilic substitution.

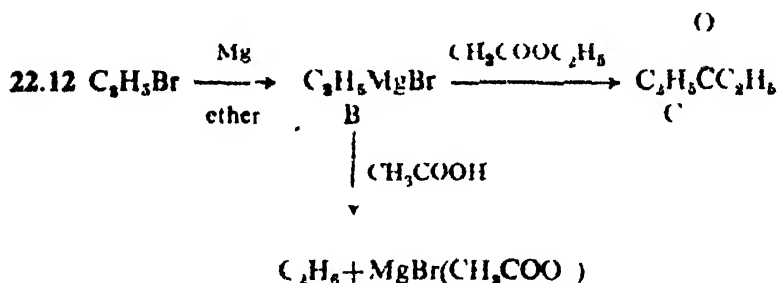
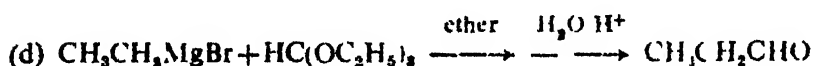
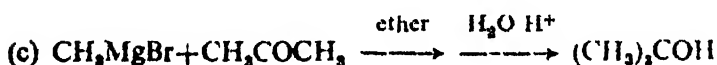
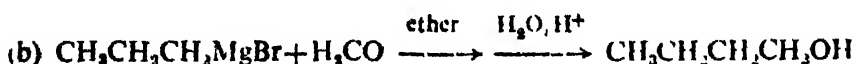
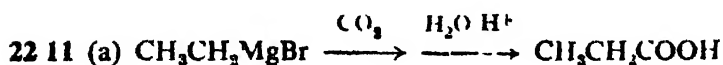
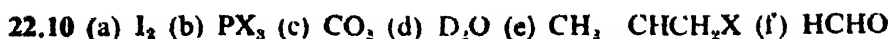
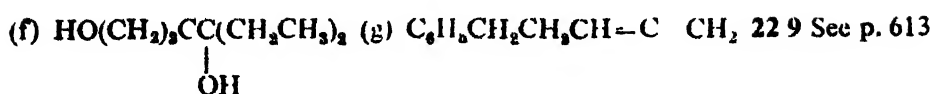
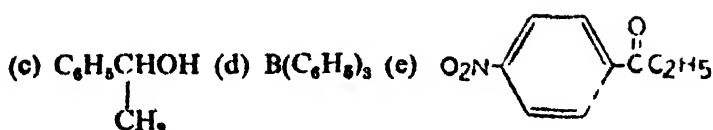
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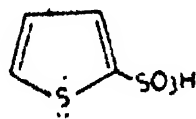
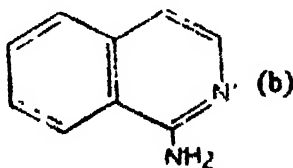


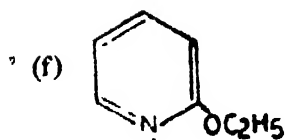
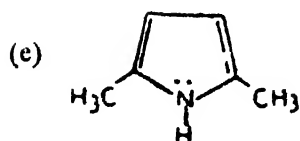
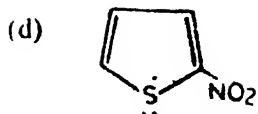
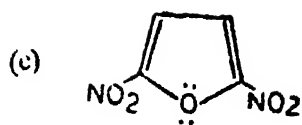


22.13 See Sec. 22.1 22.14 See the text 22.15 (a) Water gives rise to a hydrocarbon on reaction with Grignard reagent (b) No, because a Grignard reagent reacts faster with a ketone (c) yes

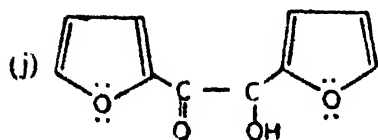
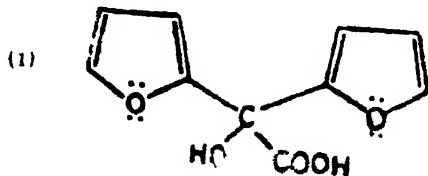
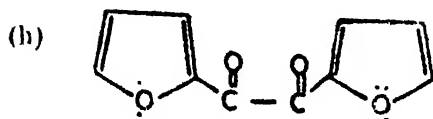
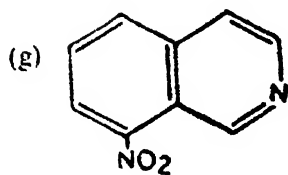
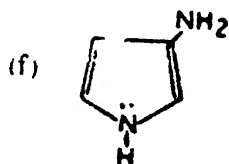
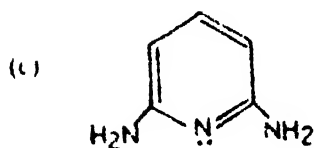
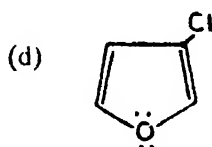
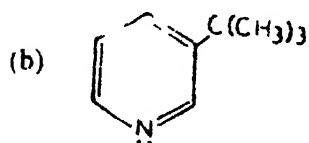
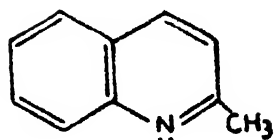
CHAPTER 23

23.1 See the text 23.2 (a)

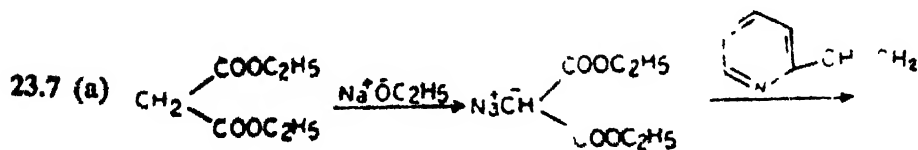


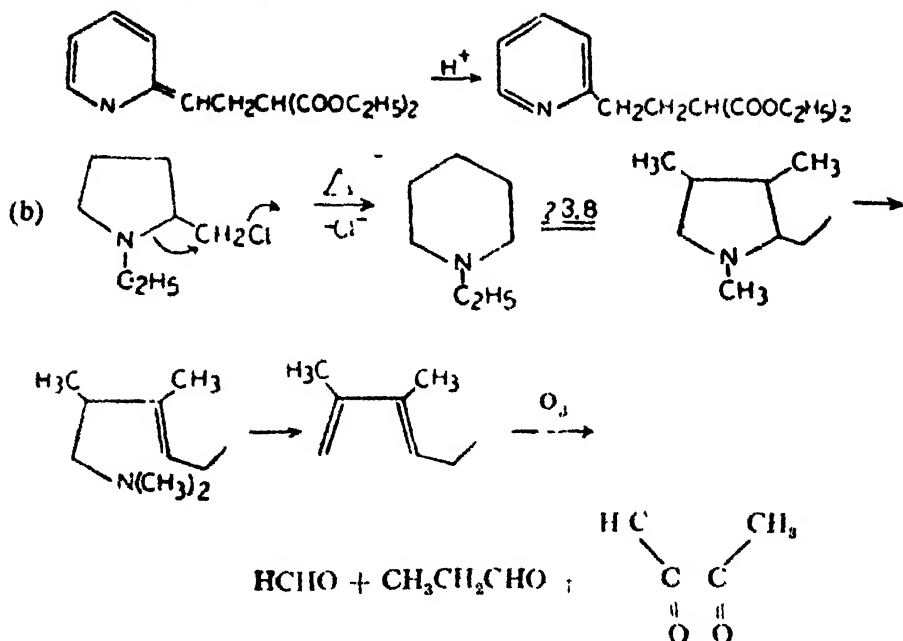


23.3 See Sec. 23.2.2 23.4



23.5 See the text 23.6 See the text





23.9 It has more electron density. 23.10 In isoquinoline, 1-position is reactive compared to position-3. 23.11 See the text 23.12 See Sec. 23.3.1 23.13 See Sec. 23.2.1. (a) It possesses an appreciable resonance energy (b) It does not undergo the D-A reaction (c) It undergoes electrophilic substitution 23.14 See the text.

23.15 *Similarities:* Both are aromatic, their amino derivatives can be diazotized and both are resistant to oxidation.

Differences: Pyridine undergoes electrophilic substitution with difficulty while benzene does so easily. Pyridine undergoes a facile nucleophilic substitution while benzene does not. Pyridine is a base while benzene is not. 23.16 See the text 23.17 See the text 23.18 See the text 23.19 See the text 23.20 See Sec. 23.3.1 23.21 (a) Because the electron pair on the nitrogen atom is delocalized into the pyrrole ring (b) The electronegative nitrogen atom decreases the electron density of the pyridine ring (c) The electron pair on nitrogen in pyrrole is not available for donation (d) Nitrobenzene is also deactivated by $-\text{NO}_2$ group (e) The ion is more stable (f) It is more diene-like (g) Site of high density (h) Less electron density on the pyridine ring (i) Pyrrole is more aromatic. 23.22 See p. 659 23.23 See the text.

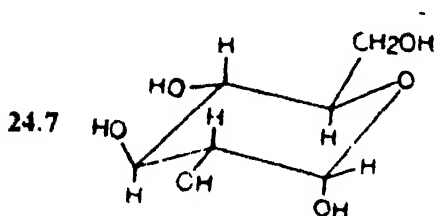
CHAPTER 24

24.1 See the text 24.2 See the text 24.3 It is customary to call a sugar as

D-sugar if the hydroxyl group next to the bottom carbon atom lies to the right, as shown below:



24.4 See the text 24.5 See the text 24.6 It does not form H—bond with water

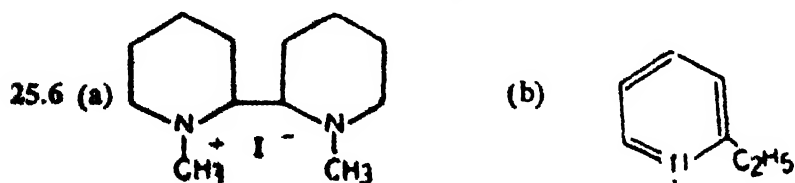


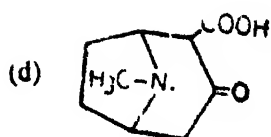
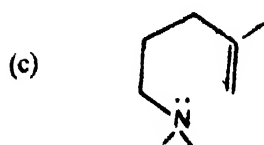
24.8 α - or β -D-fructofuranose 24.9 Sucrose—a glycoside bond; Maltose and Lactose—a hemiacetal type bond 24.10 See the text 24.11 See Sec. 24.9 24.12 Starch and cellulose 24.13 See the text 24.14 See the text 24.15 See the text 24.16 See the text 24.17 See the text 24.18 See the text 24.19 See the text 24.20 See the text 24.21 Because hydroxypyridine behaves both as an acid and a base.

CHAPTER 25



25.3 See the text 25.4 See Sec. 25.4 25.5 See Sec. 25.8

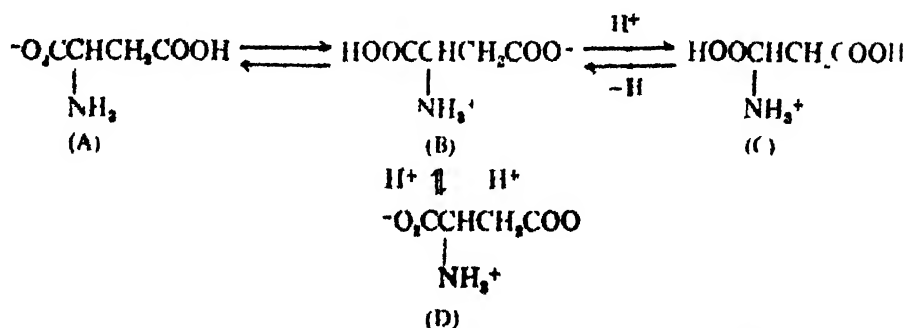




25.7 See the text 25.8 See the text

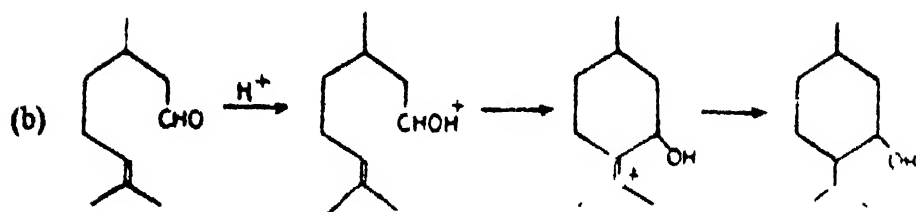
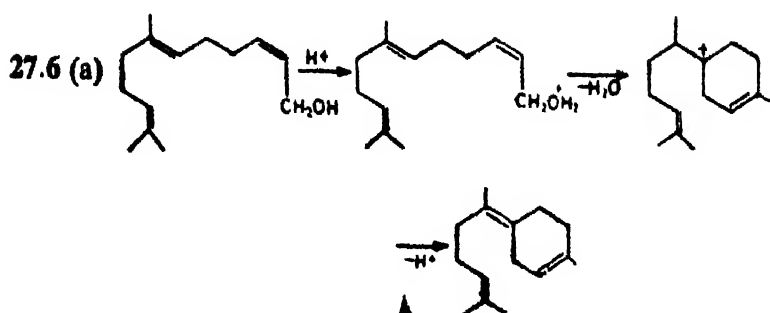
CHAPTER 26

26.1 See the text 26.2 Alanine and leucine acids (neutral) aspartic and glutamic acids (basic), lysine and histidine (acidic) 26.3 (a) $\text{H}_2\text{N}^+\text{NCOO}^-$ (b) H_2NCOOH (c) $\text{H}_2\text{NC(OH)COOH}$ 26.4 Proline 26.5 (a) Threonine give iodoform test (b) Glycine ethyl ester is alkaline towards litmus (c) Acetylphenylamine is insoluble in dil HCl (d) Aspartic acid evolves CO_2 on reaction with NaHCO_3 26.6 It has HNO_2 a secondary amino group 26.7 See the text 26.8 See the text 26.9 See the text 26.10 See the text 26.11 See the text 26.12 See the text 26.13 See the text 26.14 See the text 26.15 Amino acids are fairly soluble in water. Their solubility, however, varies with pH and is lowest at the isoelectric point. This may be due to the fact that the proximity of charges in the zwitterion (An amino acid has a maximum concentration of this ion at its pI value) are less efficiently solvated than the separated ions at low or high pH. 26.16 This may be explained by considering the following ion equilibria



As is evident ions (A) and (B) are neutral, while (C) is a cation and (D) is an anion. In species (D) the anion is derived from the second —COOH

27.3 See Sec. 27.5.1 27.4 See the text 27.5 See Sec. 27.4.



27.7 See the text 27.8 See the text.

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